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SCLERODERMA AND DERMATOMYOSITIS.*

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Terminology.

Scleroderma.—The following terms are in use :

Diffuse Symmetrical Scleroderma (Radcliffe-Crocker) or Diffuse Scleroderma.

Progressive Scleroderma.

Acrosclerosis.

Generalised Scleroderma.

Circumscribed Scleroderma or Morphoea.

The first three are used for the same syndrome, while those who speak of Generalised Scleroderma may imply either the same process or morphoea distributed widely over the body. The surface distribution of Progressive Scleroderma is in fact highly selective, not often very extensive, and limited in some instances to the fingers ; early in the disease there may no skin change. Morphoea, on the other hand, though most often localized may be distributed in large areas all over the body. Acrosclerosis was introduced into the terminology by Sellei (1934), who distinguished between a benign non-progressive disease of selective and limited distribution (acrosclerosis) and what he called true scleroderma, which was progressive and widespread. A good illustration of the latter in his paper shows that this was what some nowadays prefer to call generalized morphoea. Although it is necessary to distinguish sharply between these two processes, it has long been known that acrosclerosis is very often by no means a non-progressive illness and that however selective its surface distribution may be it is doubtful whether it is ever confined to the skin.

Terminological confusion might be overcome if we agreed to use two names : Scleroderma and Morphoea, localised or widespread.

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Dermatomyositis.—Two additional terms are sometimes used, namely poikilodermatomyositis and sclerodermatomyositis. Petges and Clejat (1906), who first accurately described chronic dermatomyositis, named the affection "atrophic sclerosis of the skin and generalised myositis", but later Petges *et al.*, (1929), believing that his case and others that he had seen in the meanwhile were identical with one described by Jacobi under the name of poikilodermia atrophicans vascularis, changed the name to poikilodermatomyositis. Dowling and Freudenthal (1938) produced evidence to show that the two affections were not identical or even related. The names sclerodermatomyositis and even acrosclerodermatomyositis have been applied to cases of scleroderma in which myasthenia has been the prominent symptom. To avoid confusion it is better to use the term scleroderma alone for such cases. As morphoea will hardly be discussed only two terms will be used throughout this paper, scleroderma and dermatomyositis.

Scleroderma.

Scleroderma is a comparatively uncommon disease; 20 cases have been treated at St. Thomas's Hospital during the past 8 years, that is 2 or 3 a year; but everyone knows the cutaneous picture, the sclerodactyly (Fig. 1), the facial immobility, and the telangiectases (Fig. 2); its selective distribution on the face, neck and the neighbouring part of the thorax, the upper limbs, especially the posterior aspect, including the dorsal tendons of the hands and fingers, and its less frequent occurrence on the lower limbs; the pigmentation and the patchy leucoderma, the commonly associated Raynaud's symptoms, and the less common calcinosis. Nothing further will be said about this aspect of the disease.

At long intervals at first, and in recent years at a rapidly increasing pace, more and more has been added to the clinical and morbid anatomical picture of scleroderma. Hutchinson (1896) drew attention to the association of what he termed "acroscleroderma" with Raynaud's phenomenon. Nixon (1903) strongly emphasised the myasthenic aspect of the disease. Thibierge and Weissenbach (1910) added calcinosis to the picture. Dysphagia must have been recognized as a part of the syndrome for many years; Radcliffe-Crocker (1902) refers to it as an occasional symptom. Matsui (1924), more than anyone else, began the acceleration in knowledge, drawing conclusions of considerable interest and importance from six comprehensive autopsies. The disease, he said, affects all the organs, and the two most frequent processes are proliferation and alteration of the connective tissue and a special modification of the small arteries which is manifest in several organs and capable of producing varied functional disturbance. The muscles are the site of various degenerative changes; in the intestines are found hypertrophy of the mucosa and atrophy

Fig. 1.

Fig. 2.

Fig. 3.

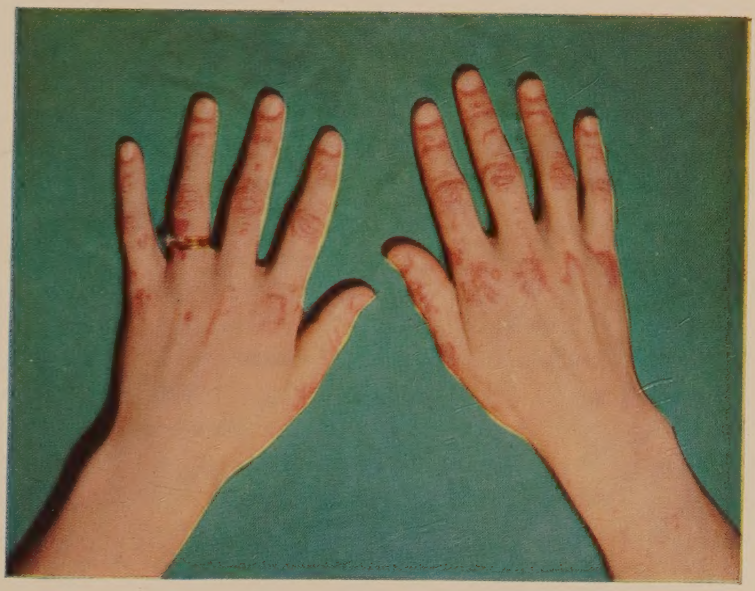

Fig. 4.

of the longitudinal muscles ; in the lungs, shrinkage with disturbance of the lesser circulation and dilatation of the right side of the heart ; in the bones osteoporosis of the terminal phalanges. Vascular changes and sclerosis of the connective tissue of the organs, he says, are the dominating processes, and although they generally coincide they are in fact independent of one another.

The Alimentary Canal.

More precise knowledge of the now well known alimentary symptoms of scleroderma and their pathology than that provided by the studies of Matsui dates from a publication by Rake (1931), whose observations have been confirmed and amplified many times. (Hale and Schatzki, 1944 ; Bevans, 1945 ; Goetz, 1945 ; Lushbaugh and others 1948 ; Skouby and Teilum, 1950 ; Prowse, 1951 ; Abrams and others, 1954).

Dysphagia.—Hale and Schatzki (1944) examined by x-rays the gastrointestinal tract of 22 patients—15 females and 7 males. Of these, 13 either complained of dysphagia or were found to have the symptom on questioning. Eleven of these and 8 without symptoms of dysphagia showed x-ray abnormalities—that is, all but 3 of the total. Barium passed into the lower part of the oesophagus with little delay, then hesitated. The abnormality was best seen with the patient in the horizontal position, giving the impression that the oesophagus had lost its peristaltic force and relied more or less on gravity to empty itself. Whimster (1954) had the opportunity of examining sections of the oesophagus of a patient with scleroderma, gross myasthenia and severe dysphagia who died almost immediately after an operation designed to relieve the dysphagia. The microscopical appearance was that of simple patchy atrophy with a minimal interstitial replacement of the muscle coats of the lower oesophagus ; the muscularis mucosae was unaffected. No sclerosis such as that observed in the dermis was observed. Dornhorst, Pierce and Whimster (1954) followed up this observation by examining six consecutive scleroderma patients by x-ray and recording the oesophageal contractions by a method described by Dornhorst, Harrison and Pierce (1954). None of these patients was aware of any difficulty in swallowing, but oesophageal function was abnormal in all. The characteristic defect was failure of the propulsive waves to continue with normal vigour. The weakness of the lower oesophagus was manifest radiographically in the supine, slightly head down position. The bolus was carried briskly to about the level of the tracheal bifurcation, where its progress ceased. Pierce has since examined 5 of my patients with no conscious difficulty in swallowing, 4 of whom show the usual defect radiographically ; in three of these the disease had developed suddenly only a few months previously. In the fifth, a woman with considerable general muscular weakness and barely perceptible scleroderma of the fingers, no defect in swallow-

ing could be demonstrated. Abrams and his associates (1954) found changes of the type described by Whimster in 3 autopsies and they also regard atrophy or complete disappearance of the external muscle fibres of the oesophagus as the essential change. Goetz (1945) described, in addition to atrophy of the outer muscle coats, ulceration and thickening of the submucosa ; but his patient had suffered from dysphagia for many years and it may perhaps be supposed that the additional changes developed later than the muscular atrophy. Lushbaugh and associates (1948), like Goetz, describe both atrophy of the muscularis and dense collagenous change in the submucosa.

Thus atrophy of the muscularis propria may perhaps reasonably be thought of as the essential cause of the functional oesophageal defect in scleroderma. It appears also that this tissue must be very frequently damaged in the process and perhaps often at a very early stage.

The intestines.—The remainder of the alimentary tract may suffer damage of the same order as that found in the oesophagus.

Rake's (1931) patient developed abdominal pain and diarrhoea two years after the onset of scleroderma ; radiographically she showed dilatation both of the small and large intestines, and the descending colon appeared to be almost completely obstructed. She died after an operation to relieve the obstruction. Four of Hale and Schatzki's (1944) 22 patients exhibited upper gastrointestinal abnormalities. These patients suffered from heartburn, gaseous eructations, a sensation of fullness in the upper abdomen, sometimes cramp-like epigastric pain, occasionally nausea and vomiting, or symptoms suggesting paralytic ileus. A point of some interest is that one of the four patients had had eructations and epigastric distress for a year before skin changes made their appearance. The radiographical findings consisted of dilatation, usually of the third part of the duodenum and of the upper part of the jejunum, with very slow emptying ; in one patient the delay extended down to the ileum. A fifth patient complained of cramp-like pain in the lower abdomen and diarrhoea, and showed radiographically peculiar sacculation of the colon. Similar changes were described in considerable detail by Goetz a year later and they have often been confirmed (Bevans, 1945 ; Skouby and Teilum, 1950 ; Prowse, 1951 ; Abrams *et al.*, 1954). A patient of mine complained of diarrhoea and abdominal distension. Radiography revealed what appeared to be an obstruction in the colon. Laparatomy disclosed gross ballooning of the intestines through the thin transparent walls of which fluid levels could be seen. The wound was closed immediately ; the patient was none the worse.

Pathology.—Goetz (1945) describes extreme atrophy of both muscular coats of the parts of the colon affected by the disease, particularly the outer longitudinal in which some of the muscle fibres were completely replaced by fibrous tissue. Abrams *et al.* (1954) found in the intestines, as in the oesophagus, loss of muscle fibres with only mild interstitial fibrosis. Skouby and Teilum

describe patchy atrophy of the intestinal and gastric musculature, and in the colon sclerosis of the submucosa by a connective tissue, poor in cells, replacing the muscularis completely. Lushbaugh and others (1948) describe similar changes. Thus on the available evidence the principal change that has been observed throughout the alimentary canal appears to be atrophy of plain muscle.

The arteries and the renal lesion.—Matsui's observations on the changes in the arteries have often been confirmed (Talbott *et al.*, 1939 ; Lewis, 1940 ; Goetz, 1954 ; Weiss *et al.*, 1943 ; Skouby and Teilum, 1950). In the arterioles the principal change is usually described as a varying degree of intimal thickening—hyaline, acellular or mucinous. Lewis (1940) examined the digital arteries of a girl with scleroderma who died of cerebral haemorrhage and whose blood urea rose shortly before death to 225 mg. per 100 c.cm. The medium-sized arteries presented moderate intimal thickening and some were completely obstructed by organized clot. This patient also had extensive necrotizing arteriolitis of the kidneys, and Lewis refers to the work of Talbott and his colleagues (1939) who a year earlier described arterial lesions in the kidney of a more advanced type. Talbott's patient had no urinary symptoms at any time and he had no reason to suspect a renal lesion, but the blood urea level was not estimated during the six weeks before death. The naked-eye appearance of the kidney was that of multiple cortical infarctions the cause of which was found in a lesion of the intralobular arteries supplying the areas of degeneration. The medullary arteries were normal, as were the arcuate arteries, but at this point the radiating intralobular arteries showed an abrupt change which ceased as abruptly at the arteriolar level. The change was an endarteritis in which the subintimal substance was infiltrated by a mucinous material which resembled Wharton's jelly. Moore and Sheehan (1952), describing the morbid anatomy of the kidneys of 3 patients who died 2 years, 4 months and 1 year respectively after the onset of scleroderma, not only confirm Talbott's observations but point out that when the specific arterial lesion develops in the kidney it damages the parenchyma severely and rapidly leads to death. The patients develop oliguria with progressive renal failure and die with some degree of uraemia within a few weeks. In addition to the peculiar mucinoid thickening of the intralobular arteries beginning at their origins that Talbott described, they found fibrinoid necrotizing changes in the peripheral parts of many of the intralobular arteries and some of the afferent arterioles. Other reports on the renal lesion in scleroderma (Banks, 1941 ; Bevans, 1945 ; Goetz, 1945 ; Weiss *et al.*, 1943) confirm its ischaemic pathology.

The heart.—Many of the autopsy reports on scleroderma are complete, but in most of them one system or a few have been specially studied. Goetz (1945) perhaps more than others has attempted to draw a complete picture of the pathology. He, Weiss and his colleagues (1943), and East and Oram (1947),

have described in detail the cardiac lesion in scleroderma and the descriptions of each, as well as of others (Davidson, 1929 ; Rake, 1931 ; Banks, 1941 ; Skouby and Teilum, 1950 ; Spain and Thomas, 1950 ; Abrams *et al.*, 1954) scattered through the literature, are so alike that the lesion must be accepted as peculiar to scleroderma. Clinically the symptoms are described as dyspnoea on exertion and sometimes orthopnoea and cyanosis, the latter usually associated however with a pulmonary lesion ; auricular fibrillation has been met with occasionally and electrocardiographic examination has usually revealed some abnormality. Radiographically, reduction in cardiac excursion has been found (Goetz, 1945). The striking feature of the naked-eye pathology is the presence of numerous streaky scars in both ventricles. Goetz describes four types of lesion based on the study of three autopsies ; (*a*) In the least involved part of the heart, muscle fibres were separated by numerous capillaries choked with blood. (*b*) There was a diffuse lesion showing separation of muscle fibres which have become interlaced by a young highly vascular connective tissue. The muscle fibres here show loss of staining power and of structure. In this type of lesion, he says, one gets the impression that it is the blood vessels which introduce the connective tissue into the muscle spaces. (*c*) Frank fibrosis of the entire thickness of the myocardium ; and (*d*) scattered foci of fibrosis among apparently normal muscle fibres. According to Weiss and his associates (1943), the scars of the heart of scleroderma are due to progressive increase of a highly vascular connective tissue accompanied by disappearance of fibres ; they could find no evidence of primary degeneration of muscle with repair. East and Oram, on the other hand, finding the same numerous small ventricular scars in their patient who died in heart failure, and histologically a vascular fibrous tissue in which isolated muscle fibres could be seen, arrive at the conclusion that for some unknown reason the cardiac muscle fibres degenerate and disappear in patches and their place is taken by new connective tissue. The cardiac muscular change appeared to them similar to that which was present in the skeletal muscles in their patient, who was in fact severely myasthenic. In all of about a dozen case histories that I have been able to find in which a cardiac lesion has been described, often very briefly as diffuse fibrosis or small linear scarring, general muscular weakness has been a prominent clinical feature, and often the common skeletal muscular changes are described in greater detail than those of the heart.

The lungs.—The earlier observation of Matsui (1924) has been followed by a number of others more recently. Some describe the clinical and radiological findings only, but in addition several full descriptions of the changes in the lungs found at post-mortem have been published. The clinical signs and symptoms have ranged from varying degrees of dyspnoea to severe pulmonary hypertension ; the radiological findings from increase in lung markings to well developed diffuse fibrosis often peripherally studded with small cysts (Rake, 1931 ; Dostrovsky, 1947 ; Getzowa, 1945 ; Goetz, 1945 ; Wigley and others,

949 ; Church and Ellis, 1950 ; Spain and Thomas, 1950 ; Kemp-Harper, 953 ; Evans and Parker, 1954). In one patient (Wigley and others, 1949) the kin was not involved until two years after the onset of pulmonary symptoms. Although the changes found at autopsy are often described in considerable detail (Rake, 1931 ; Getzowa, 1945 ; Goetz, 1945 ; Spain and Thomas, 1950 ; Skouby and Teilum, 1950 ; Evans and Parker, 1954) their development is not easy to follow. Compact fibrosis with obliteration of alveoli in some areas is described, and often more peripherally disappearance of alveoli, leaving cystic spaces often lined with cuboidal and occasionally with ciliated epithelium. The last are thought by Evans and Parker (1954) to be due to bronchiolar dilatation caused by contraction of the fibrous lung. We may possibly have seen the earliest change in a portion of lung removed by biopsy at St. Thomas's Hospital. The patient was a young man who had been suffering from general muscular weakness and loss of weight associated with Raynaud's symptoms for about nine months, and from severe dyspnoea for about three months. He was admitted under the care of Professor Sharpey-Schäfer with general myasthenia and severe pulmonary hypertension. On the backs of the fingers were some small white atrophic scars which showed histologically the changes of scleroderma of the midcorium. Radiography revealed some increase of lung markings. The following changes in the lung were found microscopically :

(i) Thickening of the alveolar walls with tortuosity of capillaries.

(ii) Partial collapse and focal slight emphysema.

(iii) Patchy fibrosis.

(iv) Degeneration of small arteries, some of which are almost obliterated by intimal hyperplasia.

(v) Phagocytosis of blood pigment in alveoli.

This patient was treated first with rest, later with corticotropin for six weeks, during which his general muscular condition improved. After two years, during which he was kept under observation as an out-patient, he had recovered most of his lost weight and all of his muscular efficiency. He was no longer short of breath, and his exercise tolerance was found to be normal. The small sclerodermatous scars and the lung markings, however, had not changed.

The thyroid.—Scattered through the literature (Hektoen, 1897 ; Matsui, 1924 ; Gordon, 1929 ; Rake, 1931 ; Jadassohn, 1931 ; Dowling, 1940) are several references to the thyroid gland, in which more or less extensive interstitial fibrotic change is usually described. This does not appear to produce functional disturbance and obviously does not influence the course of the disease in any way.

The teeth.—A wide translucent zone round the roots of the teeth was found radiologically by Stafne and Austin (1944) in 9 out of 127 cases of scleroderma. The roots of the teeth were surrounded by a soft but firmly adherent material, the back teeth were mainly affected.

The skeletal muscles.—Nixon (1903) drew attention to the frequent occurrence of severe myasthenia in scleroderma, and stated that much of the disease as it affects the muscles is totally unrelated to the distribution of the skin change. In Rake's case muscular weakness was a prominent feature, and the case so fully described by Talbott was published as one of dermatomyositis. Rake described the now well known pathology of the skeletal muscles in detail. He found in his patient every stage of degeneration—shrunken, hyaline and dark-staining fibres lying intermingled with fibres which were swollen, pale and disintegrated ; some were tortuous and whorled. In the shrunken fibres the nuclei of the sarcolemma were approximated and appeared almost as continuous lines. Talbott's description tallies exactly with Rake's, and Dowling (1938) a year later presented two cases, one with gross muscular weakness which was shortly to be the cause of death, while in the other muscular fatigue had not been experienced though the disease had been present for years. Histologically, the muscle of the first case showed extreme disintegration, but in the second was found only the minor degree of degeneration that Rake described—hyalinization of muscle bundles, absence of cross striation and increase of nuclei and their arrangement in rows along the sarcolemma. It thus appeared likely that the skeletal muscles were very often diffusely damaged in scleroderma. Muscular weakness has been in fact a prominent feature in very many of the cases described in the literature.

The clinical and pathological picture of scleroderma can now hardly be far from complete in its main outlines, but of its pathogenesis nothing is known. It is usually classified as a diffuse collagen disease and Goetz proposed a change in name from progressive scleroderma to progressive systemic sclerosis, a term which has gained some acceptance. Both Goetz's term and even the conception of diffuse collagen disease may, however, be open to criticism, since it is not clear that collagen is the only tissue which suffers damage, and sclerosis does not describe all the pathology of the disease particularly as it effects muscle, even though in the long run fibrosis may replace damaged tissue. Adams, Denny-Brown and Pearson (1954) regard widespread degeneration of muscle fibres as the striking change in skeletal muscle in scleroderma, and they are not impressed with changes in endomysial and perimysial connective tissue or in the small intramuscular blood vessels. Whimster found only atrophy of the muscular coats of the oesophagus, with minimal connective tissue replacement. In the heart, Weiss and Goetz interpret the streaky scars which they and others have so often seen as an invasion of the muscle by proliferating collagenous tissue, but East and Oram suggest that the primary change may be atrophy of the heart muscle with subsequent scarring. Though Goetz's new term correctly indicates that the process is systemic, many will no doubt prefer to retain the old name until something definite is known about its cause and pathogenesis.

Dermatomyositis.

While the changes in the skin in scleroderma are so striking that having been seen once they can hardly be forgotten, a little experience is required to recognize dermatomyositis easily. The rash, though usually characteristic, is difficult to describe ; in the opening stage erythema, often described as heliotrope in colour, and oedema, which is quite often gross, of the face, particularly of the eyelids and the malar area, are almost constantly present (Fig. 3). Puffiness in the malar area sometimes persists indefinitely, but usually it subsides slowly, leaving a reticulated telangiectatic erythema, peppered with pigmentation and depigmentation, together with the appearance of atrophy and with a certain firmness in the texture of the skin. In the long run some degree of immobility of the features resembling that of scleroderma may develop, though the taut wrinkled mouth of scleroderma is never seen in dermatomyositis (Figs. and 3). In chronic cases the scalp is sometimes invaded with permanent loss of hair, and in the majority the eruption both in the acute and chronic stages is found also on the neck, on the upper part of the chest and sometimes of the back. The same sequence of events occurs commonly on the upper limbs, especially on the posterior aspect, including the hands ; and on the fingers the eruption often closely resembles that of lupus erythematosus (Fig. 4). The lower limbs and other parts of the trunk are occasionally affected in the same way but far less often, and now and again oedema is almost universal. An analysis of 22 cases seen at St. Thomas's Hospital during the past 14 years shows that the face was affected in 21, and in addition predominantly the neck, upper thorax and upper limbs. In one case the face and both upper and lower limbs were grossly oedematous. Raynaud's symptoms were present in 3 patients and calcinosis in 4 others. Reviews of fairly large series (O'Leary and Waisman, 1940 ; Sheard, 1951 ; and Wedgwood, Cook and Cohen, 1953) illustrate the variations. Wedgwood, Cook and Cohen tabulate the clinical findings in 26 children of whom 23 had some degree of erythema and swelling of the eyelids and malar areas, and sometimes of the nose and upper lip. Changes in the skin were also prominent on the upper extremities ; the skin here appeared tight or glossy or scaly. Later, extensive atrophy was observed and at this stage the skin appeared to be tightly bound to the underlying tissues ; the fingers showed atrophy, like the atrophy of Raynaud's phenomenon. Also characteristic were lesions which occurred over the extensor surfaces of the joints, particularly the knuckles, elbows and knees. These areas appeared erythematous, atrophic and scaly with a network of fine vessels visible ; occasionally vesiculation was present ; later they often became either pigmented or depigmented. Lesions of the mucous membranes were present in two of the series. Deposits of calcium were found later in the disease in muscle, fascia and subcutaneous tissue in seven of the children.

One feature of the changes in the skin that is commonly met with in children as well as in adults is not mentioned in this accurate description, namely that the variegated atrophic change which the authors describe over bony prominences and which is often mistaken for lupus erythematosus is usually arranged in linear fashion over the knuckles and interphalangeal joints, and sometimes along the course of the tendons (Fig. 4). This highly characteristic lesion was originally described by Petges and Clejat (1906). Sheard (1951) analyses 25 cases. Of these one had no cutaneous symptoms, while in the rest the cutaneous picture conformed to the usual pattern. Calcification occurred in 4 cases, Raynaud's symptoms in 3, and a scleroderma-like change on the face, neck and forearms in 3. In their well known earlier analysis of 40 cases O'Leary and Waisman (1940) paint a similar cutaneous picture. Scleroderma-like change occurred in 7 of these patients, Raynaud's symptoms in 10 and calcinosis in 5. These analyses indicate that there is an elective distribution of the eruption in dermatomyositis, and that its character is not ill defined.

Muscular symptoms vary from extreme prostration with difficulty in deglutition and occasionally with nasal speech, to a degree of myasthenia of which the patient is hardly conscious. In the last few months I have had under my care a woman aged 24 who has had swelling and erythema of the face and the characteristic telangiectatic atrophy over the posterior aspect of the elbows, over the knuckles and interphalangeal joints, for 16 years. She has served in the Royal Air Force for two years and she has never been conscious of any disability except the mild skin symptoms. Some loss of muscular power can, however, be demonstrated, and during a short stay in hospital her creatine excretion on one occasion was 375 mg. in 24 hours. Histologically the skin over the point of the elbow shows scleroderma of the upper dermis.

Langmead (1923) was led to the conclusion that on the evidence at that time available a single morbid process underlies scleroderma and dermatomyositis. In support he recalled the relatively common occurrence of Raynaud's symptoms in dermatomyositis, the frequency of oedema in the opening stage of scleroderma as in dermatomyositis, of occasional fever in the early stage of scleroderma, of calcinosis in dermatomyositis and in particular the muscular symptoms in scleroderma to which Nixon had drawn attention and which differed in no way from those found dermatomyositis. Dowling (1940) pointed in addition to the commonly similar distribution of the skin change in the two diseases, and to the common histological finding of flattening of the epidermis and of homogenization of the subepidermal collagenous tissue in dermatomyositis. Banks (1941) lent further support to this point of view, postulating a common denominator between scleroderma, dermatomyositis, lupus erythematosus and polyarteritis nodosa. At that time the reports of Matsui, Rake and Talbott were available, but the visceral pathology of scleroderma had not been as fully described and it was not as well known as it is now. If Langmead's view is

orrect, post-mortem studies in dermatomyositis will reveal changes in the nternal organs similar to those of scleroderma. They have not done so. Three of 13 such reports (Moore and Koch, 1928 ; Sheldon *et al.*, 1939 ; Marcus nd Weinstein, 1935 ; Karelitz and Welt, 1935 ; Wolf and Wilens, 1936 ; Lane, 1938 ; Kinney and Maher, 1940 ; McCombs and McMahon, 1947 ; Wainger and Lever, 1949 ; Sheard, 1951 ; Lugt, 1952 ; Cottel, 1952 ; Wilson, 954 ; Mendeloff, 1954) describe cardiac lesions, focal necrotic change in groups of muscle cells (Mendeloff), multiple foci of mucoid degeneration of interstitial connective tissue, surrounding, compressing and apparently producing degeneration of individual myocardial fibres (Wainger and Lever) and marked degeneration of cardiac muscle in patches (Kinney and Maher). Two describe intimal hickening of small arteries (Wainger and Lever, Kinney and Maher), four ulceration in the intestinal canal (Wainger and Lever, Karelitz and Welt, Marcus and Weinstein, Moore and Koch), in two of which the ulcers were attributed to occlusion of vessels at the base of the ulcers (Wainger and Lever, Moore and Koch). Others describe only changes in the skin and muscles, and those of a erminal infection, usually pneumonia. Of five autopsies on the series seen at St. Thomas's Hospital since 1946, in one, a young policeman who was almost prostrate for nearly three years, and who died with miliary tuberculosis, Dr. Whimster found slight atrophy of the myocardium, atrophy of the muscle coats of the lower end of the oesophagus, which however had undergone some degree of post-mortem autolysis, and large ulcers in the colon and rectum. The remaining 4 disclosed no pathological changes other than those commonly found in the skin and muscles.

Throughout the literature the epidermis is usually described as flattened, while the subepidermal connective tissue is condensed, hyalinized, homogenous, or mucoid in appearance. Adams, Denny-Brown and Pearson (1954) do not differentiate between the type of change found in the skeletal muscles of acute or chronic dermatomyositis and scleroderma. Two post-mortem reports (Horn, 1941 ; Davison, 1929) describe morbid anatomical changes in chronic dermatomyositis which are identical with those found in scleroderma—fibrotic lung with dilatation of terminal bronchioles and gross dilatation of the duodenum in one, small fibrotic scars in the cardiac muscle in the other. These would establish the identity of the two processes without question, but the case histories of both are characteristic of scleroderma.

It appears in fact that the morbid anatomical changes in the two diseases correspond frequently only in the muscles and in the skin, and that in the skin condensation of collagen bundles is more superficial in dermatomyositis than in scleroderma. In other organs only Wainger and Lever's observations of mucoid degeneration of interstitial connective tissue in the myocardium and Whimster's of atrophy of the muscle coats of the lower end of the oesophagus in

one case of chronic dermatomyositis, are at all similar to the visceral changes so often met with in scleroderma.

Cancer and Dermatomyositis.

During the past twenty years a considerable number of case histories and autopsies have been reported which point to the somewhat frequent association of dermatomyositis with visceral malignant disease. Schuermann (1951), reviewing 336 published cases of dermatomyositis, found among them 31 with associated malignant growth. Subjecting these figures to statistical analysis he finds that the incidence of malignancy in dermatomyositis is five times that in the normal population. He found no record of malignancy in his own practice and in the current literature over a period of 20 years in 600 cases of progressive scleroderma. The histories in the majority of 25 published cases that I have read consecutively (Savill, 1939, 1 case ; Bezecny, 1935, 2 cases ; Pick, 1935, 1 case ; Sheldon *et al.*, 1939, 1 case ; Behrman and Forman, 1939, 4 cases ; Dostrovsky and Sagher, 1946, 2 cases ; McCombs and McMahon, 1947, 1 case ; Lipman and Tober, 1950, 1 case ; Sheard, 1951, 3 cases ; Brunner and Lobraico, 1951, 1 case ; Lugt, 1952, 1 case ; Cottel, 1952, 2 cases ; Duverne, Bonnayme and Mounier, 1954, 1 case ; Wolf and Wilens, 1936, 1 case ; Bergougoran and Arne, 1947, 1 case ; Wainger and Lever, 1949, 1 case ; Lane, 1938, 1 case) are all very similar (see Table). In nearly all the symptoms have been acute with a good deal of oedema and severe muscular weakness, but in a few the skin changes have been those of chronic dermatomyositis. In all, malignancy appears likely to have preceded the onset of dermatomyositis. In 4 cases (Bezecny, Brunner and Lobraico, Duverne and others) treatment of the malignancy by operation or by radiotherapy is said to have been followed by improvement in or disappearance of the cutaneous and muscular symptoms. The symptoms have followed the characteristic muscular and cutaneous pattern, and they evidently have not differed from acute or chronic dermatomyositis unassociated with malignancy. Three of the comparatively recent series of 20 cases at St. Thomas's Hospital have had associated malignant disease, one ovarian and two pulmonary. In one, a patient of Dr. J. B. Harman, an ovarian carcinoma preceded the dermatomyositis by 15 months. In the second, under the care of Dr. John Anderson, a small lung shadow was discovered at the time of admission to the hospital, and this increased in size during the course of the illness. This patient also had Raynaud's symptoms. He died of dermatomyositis in just under two years after the onset of the disease, and at autopsy he was found to have a bronchial carcinoma. The third patient, a man of 64, who was under my care, presented himself in the out-patient department one afternoon with acute livid telangiectatic erythema together with gross oedema of the face and arms. He had spent the previous day sailing a dinghy and he had been perfectly fit up to the day of admission. The diagnosis of

Author.	Age and sex of patient.	Type of eruption.	Type of malignancy.	Time of diagnosis of malignancy in relation to onset of dermatomyositis.	Course of dermatomyositis.
Bezecny	(1) F. 58	Acute erythematous	Carcinoma of both ovaries with metastases in the peritoneum and thorax	Carcinoma discovered 9 months after onset of dermatomyositis	Recovery after surgical removal of main tumours.
	(2) F. 41	Erythematous and oedematous	Carcinoma of both breasts	Carcinoma found at post-mortem	Died 4 days after admission to hospital.
Pick	F. 44	Acute but later chronic type of skin change	Carcinoma of both ovaries with metastases in visceral and parietal peritoneum, liver and muscles of thorax	Carcinoma discovered at post-mortem. Never examined gynaecologically because nothing pointed to it.	Died 4 months after onset of dermatomyositis, of pneumonia and cardiac failure.
Sheldon	M. 17	Acute erythematous and oedematous	Reticulosis mediastinum	Autopsy	Death from dermatomyositis 5 months after onset of symptoms.
Behrman and Forman	(1) M. 62	Chronic dermatomyositis	Carcinoma of stomach	Gastrectomy before onset of dermatomyositis, subsequent metastases	Alive 6 months after onset.
	(2) F. 60	Acute followed by chronic change	Inoperable carcinoma of breast	Five months preceding onset of dermatomyositis	Not stated.
	(3) F. 51	Acute erythematous	Squamous epithelioma found in glands, primary source not discovered	Preceded onset of dermatomyositis by 4 months	Died in about 4 months
Savill	F. 58	Acute erythematous oedema of face	Carcinoma vagina	Treated by radiotherapy four months before onset of dermatomyositis	Recovered from dermatomyositis in about 6 months, but subsequently died of malignant growth.
Wolf and Wiiens	M. 53	Acute erythematous	Carcinoma of gall bladder with local secondary deposits	Autopsy	Died three months after onset of symptoms.
Lane	F. 32	Acute erythematous	Carcinoma of breast with metastases	Preceded dermatomyositis by 5 months	Died 2½ months after onset
Duverne *et al.*	F. 34	Chronic Petges-Jacobi type	Carcinoma of uterus—inoperable and extensive	Discovered during illness	Temporary improvement followed treatment of carcinoma by radiotherapy.
St. Thomas's Hospital. Harman	F. 52	Acute erythematous and oedematous	Adenocarcinoma arising from ovaries	Preceded dermatomyositis by 15 months	Died 6 months after onset of dermatomyositis
Anderson	M. 60	Acute followed by subacute	Carcinoma of bronchus	Found radiographically on admission for acute dermatomyositis. Confirmed at autopsy	Died 2 years after onset of acute illness.
Dowling	M. 64	Acute erythematous and oedematous	Carcinoma of lung with secondary deposits in regional glands	Autopsy	Died 6 weeks after onset of dermatomyositis.
Cottel	(1) M. 50	Erythematous and oedematous	Large carcinoma of stomach	Found at operation	Died 6 months from onset of dermatomyositis.
	(2) M. 58	Generalized oedema	Adenocarcinoma of kidney	Autopsy	Died 5 weeks after onset of dermatomyositis.
Bergouignan and Arne	M. 58	Oedematous at first later subsiding	Carcinoma of stomach	Palpable tumour discovered a year after the onset of dermatomyositis	Died 13 months after onset of dermatomyositis.
Lipman and Tober	(1) F. 52	Oedematous primarily described as waterlogged, subsequently subsiding, change described as scleroderma	Adenocarcinoma of rectum	Preceded the onset of acute illness by more than five months	Still living at time of report.
	(2) M. 55	Oedematous	Carcinoma of stomach	Operation preceded the onset of dermatomyositis by 1 month	Died 5 weeks after onset of dermatomyositis.
Lugt	F. 61	Acute erythematous and oedematous	Adenocarcinoma of stomach invading other organs	Autopsy	Died in less than 1 month.
Wainger and Lever	M. 76	Acute erythematous and oedematous	Carcinoma of stomach	Autopsy	Died 3 months after onset of symptoms.
Dostrovsky and Sagher	(1) F. 33	Acute oedematous followed by chronic	Haemangioendothelioma of breast	Discovered 4 months before onset of dermatomyositis	Died in about 5 years.
	(2) F. 65	Acute erythematous and oedematous	Ovarian tumour	Observed clinically during the illness	Died about 3 months after onset of dermatomyositis.

dermatomyositis was made rather than acute lupus erythematosus because of the oedema. Within a few days he was completely prostrate and he died within six weeks of the day of onset of the illness. A carcinoma of the size of a small pea at the periphery of the lung with secondary deposits in regional glands was discovered at autopsy. The muscles were completely disintegrated.

The principal facts are assembled in the accompanying table which appears strongly to support a relationship between malignancy and dermatomyositis when they are associated. It is also seen that the order of events has been malignancy followed by dermatomyositis, and that when death has occurred, dermatomyositis and not malignancy has been the cause in almost every case.

Considering the points of resemblance between scleroderma and dermatomyositis —the similar distribution of the skin change in both, the oedema common to both, the gradual development of scleroderma-like hardening of the skin in chronic dermatomyositis, and histologically the condensation of collagen in the upper dermis even early in the disease—it is difficult to believe that no link between the two exists. To the similarity of the skin phenomena may be added the comparative though unequal frequency of Raynaud's symptoms and of calcinosis in both, but above all the identity of the muscular pathology in the two disorders.

But developments in the past twenty years have accentuated well marked divergences and there cannot now be much doubt that until we have some positive knowledge of the pathogenesis of the two processes, it is wiser to regard them as separate diseases. Differential diagnosis presents no great difficulty. The grip is never restricted in dermatomyositis, the mouth never becomes taut, difficulty in deglutition is common to both diseases, but the propulsive mechanism of the oesophagus proper and of the rest of the alimentary canal is probably disturbed only in scleroderma. Calcinosis occurs in both but its distribution is different—knuckles, finger joints, elbows and other bony prominences in scleroderma : subcutaneous tissue, fascia and muscles in dermatomyositis. Finally, there is the remarkable association of malignancy with one disease and not with the other.

Natural History.

However important it may be to do so, it appears to be quite impossible to predict the course of any case of dermatomyositis. The few series that have been published indicate, however, that about half of the patients die within a relatively short period, from a few weeks to a few years. Of those that do not die, a proportion evidently recover completely while in the remainder the disease persists indefinitely. The remissions and relapses that are sometimes described are probably more accurately interpreted as fluctuations. In their very careful analysis of 26 cases in children between the ages of 2 and 11,

Wedgwood, Cook and Cohen relate that 10 died, 8 recovered and were able to lead normal active lives, 4 had active disease at 1 to 5 years after the onset of the disease, and the remaining 4 were crippled by contractures.

O'Leary and Waisman were able to follow up 38 cases, of whom 19 died, 4 recovered completely, and of the remaining 15 some improved up to a point and became stationary while others went gradually downhill.

Of Sheard's series of 25 cases, 13 died after an average period of twenty months. No account of the fate of the 12 surviving cases is given.

Dermatomyositis, like scleroderma, is usually classified as a diffuse collagen disease, and the literature shows that the points of similarity between the two are generally recognized. But the term collagen disease does not apply satisfactorily to the most characteristic feature of dermatomyositis, which is the more or less severe degeneration of muscle. No doubt the general epithet of diffuse collagen disease has come to stay, though I understand that Klemperer, who invented the conception, no longer approves of it whole-heartedly. My colleague Dr. Whimster tells me that on the basis of embryology the tissues which, as far as it is possible to judge, are primarily damaged in both processes, may be included in the broader term mesodermal.

Morphoea.

Morphoea has not been discussed partly because of lack of time, but also because at the present there is not very much that one can usefully say about it. As far as I know at the present time, the widespread visceral changes that are found in progressive scleroderma have not been found in morphoea, however widely distributed. It is true that in the earlier stage of a widespread attack a degree of general myasthenia comparable with that so often met with in progressive scleroderma may occur ; Addison described the association about a hundred years ago. But the fact that the disease has remained mainly the concern of the departments of dermatology, of physical medicine, and occasionally of orthopaedic surgery, perhaps indicates that its pathology is relatively restricted. None the less the pathology of the skin as far as it is possible to judge by histology is the same in both processes, and it is possible that the material, always readily provided by morphoea, may be one of the best available for future investigation.

I believe it is doubtful whether the normal morbid anatomical approach will advance knowledge much further. Research in this field may require new technical resources. I know of only one attempt in this direction, a piece of work performed recently by Musso (1954) at the Institute of Dermatology. His work appears to show that the first change in scleroderma is the laying down of an excess of ground substance and that new bundles of collagen fibres may be elaborated from this amorphous substance. If this observation is

correct it supports the belief so long held by morbid anatomists that scleroderma as far as it concerns collagenous tissue is a proliferative process. This was a tiny step but perhaps in the right direction.

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STANDARD PATCH TESTS IN ECZEMA AND DERMATITIS.

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It has been shown that patch tests performed with a routine series of potential allergens give more positive reactions on a group of eczematous subjects than they do on a similar group of normal controls (Jaeger, 1923 ; Bloch and Jaeger, 1931). Moreover, patients with contact dermatitis tend to give more positives than those suffering from constitutional eczema (Rostenberg and Sulzberger, 1937). It has therefore been presumed that the epidermis of eczematous subjects shows some degree of polysensitivity to contact allergens which is most pronounced in those suffering from contact dermatitis. However, the substances which give these positive reactions do not always produce clinical skin disease under ordinary conditions of exposure (Sulzberger, 1940) and some positives may be explained as resulting from a lower threshold of general reactivity in eczematized than in normal skins (Morris, 1953).

Attempts to induce sensitivity experimentally with two simple chemicals showed that 50% of subjects with active contact-type dermatitis became sensitized to both the chosen allergens, compared with 23·5% of patients with questionable contact-type dermatitis and 12·5% of those without contact-type dermatitis (Sulzberger and Rostenberg, 1939). In spite of this it was found (Landsteiner, Rostenberg and Sulzberger, 1939) that some persons highly susceptible to sensitization with one chemical showed little or no susceptibility to sensitization with another chemical ; and guinea-pigs sensitized to 2-4-dinitrochlorbenzene showed no greater tendency to become subsequently sensitized to ragweed than did previously unsensitized animals (Ginsberg *et al.*, 1939). It would appear, therefore, that although the eczematous patient is more likely to give a positive patch test to any given allergen than is a normal control, this cannot be unreservedly accepted as evidence of a greater tendency to epidermal sensitivity.

The present investigation was undertaken to determine whether in fact more positive reactions were obtained in eczematous subjects than in normal controls, and to try to discover whether these positives indicate true epidermal allergy or merely a non-specific state of increased reactivity.

The Present Investigation.

This consisted of the performance of patch tests with the following substances on a series of normal and eczematous patients :

(1) Nickel sulphate . . . 5 % in water.
(2) Sodium arsenate . . . 10 % ,, ,,
(3) Ammoniated mercury . . 5 % ,, soft paraffin.
(4) Potassium dichromate . . 0·5% ,, water.
(5) Procaine hydrochloride . . 2 % ,, ,,
(6) Formalin . . . . 6 % ,, ,,
(7) Potassium iodide . . . 50 % ,, soft paraffin.
(8) Paraphenylene diamine . . 1 % ,, ,, ,,
(9) Oil of turpentine . . . 50 % olive oil.
(10) Tincture of pyrethrum

The concentrations used are those suggested by Rostenberg and Sulzberger (1937) and Sulzberger (1944).

The patches were removed after forty-eight hours and read, doubtful reactions being read again after an interval of fifteen minutes. The clinical material consisted of fifty patients with eczematous contact dermatitis, fifty with discoid (nummular) eczema, fifty with atopic eczema and fifty normal subjects. Patients with acute and extensive eczema and those exhibiting group sensitivity were not included. The patients with contact dermatitis were all believed to be suffering from allergic sensitivity, the sensitizing agents being : Nickel (12), penicillin (5), streptomycin (5), chrysanthemum (4), lipstick (4), chromates (4), rubber (4), primula (3) ; and in one case each, face powder, lubricating oil, hair cream, tulle gras, acriflavine, amidol, mercury, lanoline, and mahogany.

They were thirty-two males and eighteen females of an average age of 38·9.

The patients with discoid eczema consisted of thirty-one males and nineteen females, their average age being 40·4.

The atopics were twenty-five males and twenty-five females, average age 26.

The normal subjects were thirty males and twenty females, average age 49·1.

Results.

These are summarized in Table I.

Table I.—*Positive Reactions Expressed as Percentages.*

	Nickel sulphate.	Sodium arsenate.	Hydrarg. ammon.	Pot. dichromate.	Procaine.	Formalin.	Potassium iodide.	Paraphenylene diamine.	Oleum terebinth.	Tinc. pyrethrum.	Total.
Contact	13·2	52	51	21·3	16	10	46	8	0	16	23·7
Discoid	4	34	42	12	6	8	18	8	0	8	14
Atopic	16	64	18	18	0	2	20	4	6	2	15
Normal	0	14	18	0	0	4	14	6	6	6	6·8

Of the 500 tests in each group positive reactions were given by 34 (6·8%) of normals. 75 (15%) of atopics. 70 (14%) of discoid eczemas and 115 (23·7%) of patients with contact dermatitis.

The weakest allergic reaction produces erythema covering the area of the patch test. without oedema, papules or vesicles. Such a reaction is often seen when patch testing with face powder in a sensitive subject. This was accepted in the present series as a minimal positive reaction.

"Positive" reactions were given by 14·9% of all patch tests. Included among them are some follicular responses given to metals by atopic subjects. These were provisionally accepted as positives although it was thought that they were not allergic reactions. The high total of positive readings suggested that many of the erythematous or erythemato-oedematous reactions were also probably irritant rather than allergic.

It is often possible to distinguish between a primary irritant and an allergic reaction by retesting after an interval of a few weeks, using serial dilutions of the test substance. When this is done one of the following patterns is usually seen :

(i) *The true allergic reaction*. often producing erythema, oedema and small vesicles in strong concentrations. diminishing very gradually as the test substance is diluted. In all cases of confirmed allergic sensitivity positive reactions were still obtained after the test substance had been diluted to 10% of its original strength (Fig. 1).

(ii) *The irritant reaction* causing erythema. erythema and oedema, follicular

FIG. 1.—Streptomycin dermatitis. Positive reactions to streptomycin in aqueous solution : (1) ½%, (2) 1%, (3) 2½%, (4) 5%.

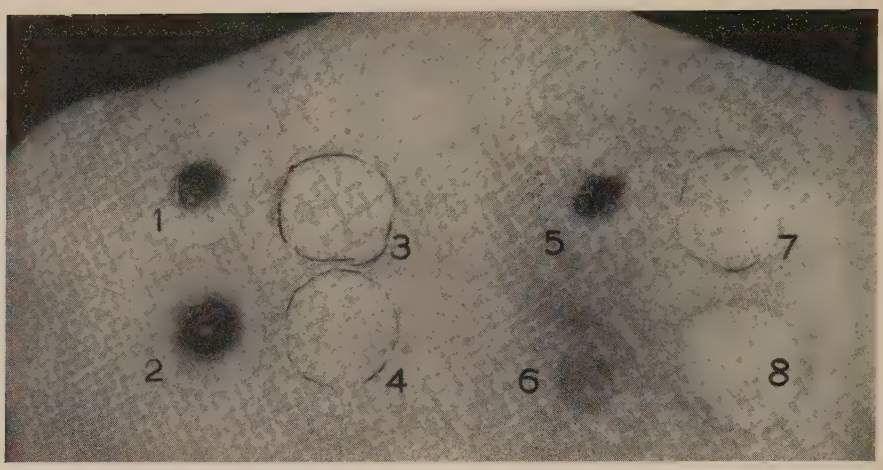

Fig. 2.—(1) (2) (5) Primary irritant reactions to samples of furniture polish. (3) (4) (7) Negative reactions to 50% dilution of furniture polish in olive oil. (6) Allergic reaction to face powder. (8) Negative reaction to face cream.

papules or necrosis in strong concentrations, but usually fading quickly as the test substance is diluted. A patient, for example, giving necrotic reactions to three different furniture polishes (Fig. 2) gave no reaction to the same polishes diluted to 50% with olive oil. An atopic subject giving a strong pustular reaction to 5% nickel sulphate gave no reaction to 2·5% nickel sulphate.

(iii) *A "non-specific false positive."*—This reaction consists of erythema and occasionally oedema appearing with some dilutions and not with others and bearing no quantitive relationship to the strength of the test substance. This irrational behaviour and the negative results of usage tests suggest that this is not an allergic reaction.

Retesting.

A small group of fourteen patients, six with allergic contact dermatitis and eight with atopic eczema, were retested with the same substances in full strength and in a half, quarter, and a tenth of the original dilutions. The results are given in Tables II and III.

The contact dermatitis group on retesting gave positive reactions to all dilutions of the substance believed to have caused their dermatitis. One penicillin dermatitis subject gave a delayed reaction to the lowest dilution of penicillin (50 O.u./ml.) with immediate positive reactions to higher concentrations. One streptomycin-sensitive subject showed no immediate reaction on retesting to streptomycin but all dilutions gave positive reactions two days after the patches were removed. In this group of six patients there were originally 23 positives out of the 60 routine tests. Twenty-one of these were repeated and it was found that on retesting 11 of the original positives were negative in

TABLE II.—*Serial Patch Tests in Contact Dermatitis.*

Initial.	Sex.	Date.	Chrysanth. oily extract. (%).	Penicillin 500 O.u/ml. (%).	Streptomycin (%).	Nickel sulphate (%).	Sod arsenate (%).	Hydrarg. ammon. (%).	Pot. dichromate (%).	Procaine (%).	Formalin (%).	Pot. iodide (%).	Paraphenylene diamine (%).	Ol. terebinth (%).	Tinc. pyrethrum (%).
M. F—	F.	27.ix.53	—	100+++	5 +	—	—	—	—	—	—	—	—	—	—
Penicillin		31.x.53	—	—	—	—	10 +	5 +	—	2 +	—	50 +	—	—	100+
dermatitis		29.v.54	—	100++	5 +	—	10 +	5 −	—	2 +	—	50 −	—	—	100−
			—	50+	2·5 +	—	5 +	2·5 −	—	1·0 +	—	25 +	—	—	50−
			—	25++	1·25+	—	2·5+	1·25−	—	·5 +	—	12·5+	—	—	25+
			—	10+	·5 +	—	1·0+	·5 −	—	·25+	—	5 −	—	—	10−
S. P	F.	22.i.54	—	—	5 ++	—	10 +	—	—	—	—	50 +	—	—	—
Streptomycin		21.v.54	—	—	5 ++	—	10 +	—	—	—	—	50 +	—	—	—
dermatitis			—	—	2·5 ++	—	5 −	—	—	—	—	25 +	—	—	—
			—	—	1·25++	—	2·5−	—	—	—	—	12·5	—	—	—
			—	—	·5 +	—	1 −	—	—	—	—	5 −	—	—	—
T. D—	M.	22.i.54	100++	—	—	5 +	10 +	5 +	—	2 +	—	50 +	—	—	100+
Chrysanthemum		6.v.54	100++	—	—	5 −	10 −	5 −	—	2 −	—	50 +	—	—	100−
dermatitis			50++	—	—	2·5 −	5 −	2·5 +	—	1·0 −	—	25 −	—	—	50−
			25++	—	—	1·25−	2·5−	1·25+	—	·5 −	—	12·5−	—	—	25−
			10++	—	—	·5 −	1·0−	·5 −	—	·25−	—	5 −	—	—	10−
J. S—	F.	29.i.54	—	—	5 ++	—	10 +	—	—	—	—	50 +	—	50 +	—
Streptomycin		16.vi.54	—	—	5 +	—	10 −	—	—	—	—	—	—	50 −	—
dermatitis			—	—	2·5 +	—	5 −	—	—	—	—	—	—	25 −	—
			—	—	1·25+	—	2·5−	—	—	—	—	—	—	12·5−	—
			—	—	·5 +	—	1·0−	—	—	—	—	—	—	5 −	—
O.H—	F.	20.ii.54	—	100+	—	—	10 ±	—	·5 +	2 +	—	50 +	—	50 ±	100
Penicillin		29.v.54	—	100+	—	—	—	—	·5 −	2 −	—	50 −	—	50 −	—
dermatitis			—	50+	—	—	—	—	·25 −	1·0 −	—	25 −	—	25 −	—
			—	25+	—	—	—	—	·125−	·5 −	—	12·5−	—	12·5−	—
			—	10+	—	—	—	—	·05 −	·25−	—	5 −	—	5 −	—
C. P—	F.	10.iii.54	—	—	5 ++	—	—	—	—	—	—	50 +	—	50 +	—
Streptomycin		7.v.54	—	—	5 ++	—	—	—	—	—	—	50 +	—	50 +	—
dermatitis			—	—	2·5 +	—	—	—	—	—	—	25 ±	—	25 ±	—
			—	—	1 +	—	—	—	—	—	—	12·5−	—	12·5−	—
			—	—	·5 ++	—	—	—	—	—	—	5 −	—	5 −	—

TABLE III.—*Serial Patch Tests in Atopics.*

Name.	Sex.	Date.	Nickel sulphate (%).	Sodium arsenate (%).	Hydrarg. ammon. (%).	Pot. di-chromate (%).	Pro-caine (%).	Forma-lin (%).	Potassium iodide (%	Para-phenylene diamine. (%).	Oleum terebinth (%).	Tinc. pyrethrum (%).
L. F—	M.	20.iii.54	—	10 ++	—	—	—	—	—	—	—	—
		22.iii.54	—	5 —	—	—	—	—	—	—	—	—
			—	2·5 —	—	—	—	—	—	—	—	—
			—	1 —	—	—		—	—	—	—	—
D. S—	M.	6.iii.54	—	10 +	5 +	—	—	—	50 +	1+	—	—
		20.iii.54	—	5 ±	2·5 —	—	—	—	—	—	—	—
			—	2·5 —	1	—	—	—	—	—	—	—
			—	1 —	—	—	—	—	—	—	—	—
D. W—	F.	6.iii.54	—	10 +	—	—	—	—	—	—	—	—
		7.v.54	—	10 —	—	—	—	—	—	—	—	—
			—	5 +	—	—	—	—	—	—	—	—
			—	2·5 +	—	—	—	—	—	—	—	—
			—	1 —	—	—	—	—	—	—	—	—
J. W—	M.	5.xii.53	5 +	10 +	—	—	—	—	—	—	—	—
		7.v.54	5 ±	10 ±	—	—	—	—	—	—	—	—
			2·5 —	5 —	—	—	—	—	—	—	—	—
			1·25—	2·5 —	—	—	—	—	—	—	—	—
			·5 —	1·0 —	—	—	—	—	—	—	—	—
J. D—	M.	24.ii.54	5 ++	10 +	—	·5 +	—	5 +	50 +	—	—	—
		26.v.54	5 —	10 —	—	·5 —	—	5 —	50 —	—	—	—
			2·5 —	5 —	—	·25 —	—	2·5 —	25 —	—	—	—
			1·25—	2·5 —	—	·125—	—	1·25—	12·5—	—	—	—
			·5 —	1·25—	—	·05 —	—	·5 —	5 —	—	—	—
L. T—	M.	20.ii.54	5 ++	10 +	—	·5 +	—	—	—	—	—	—
		16.vi.54	·5 —	10 +	—	·5 —	—	—	—	—	—	—
			2·5 —	5 —	—	·25 —	—	—	—	—	—	—
			1·25—	2·5 —	—	·125—	—	—	—	—	—	—
			·5 —	1·25—	—	·05 —	—	—	—	—	—	—
R. S—	M.	28.xi.53	5 +	10 +	—	—	—	—	—	—	—	—
		29.v.54	5 +	10 +	—	—	—	—	—	—	—	—
			2·5 —	5 +	—	—	—	—	—	—	—	—
			1 —	2·5 —	—	—	—	—	—	—	—	—
			·5 —	1 —	—	—	—	—	—	—	—	—
D. B—	M.	5.xii.53	5 +++	10 ++	—	·5 +	—	—	—	—	—	—
		29.v.54	5 —	10 +	—	·5 —	—	—	—	—	—	—
			2·5 —	5 —	—	·25 —	—	—	—	—	—	—
			1 —	2·5 —	—	·125—	—	—	—	—	—	—
			·5 —	1 —	—	·05 —	—	—	—	—	—	—

ll dilutions, 5 appeared to be of primary irritant type and 3 adopted a "non-pecific false positive" pattern. Retesting over the site of a previous positive eaction was a possible cause of some of these false positives. Of the 21 outine tests there was only one definite and one doubtful allergic pattern. oth of these were given by M. F—, a penicillin-sensitive nurse aged 33 who ave positive reactions to all dilutions of penicillin, sodium arsenate, procaine nd also to streptomycin. No erythema was produced by painting sodium rsenate for three days on an unoccluded area of skin and the reactions to this ubstance were believed to be primary irritant ones. The consistently positive eactions to all dilutions of procaine and streptomycin were considered to be llergic and she was the only subject retested who showed unequivocal evidence f polysensitivity.

The atopic group originally gave 21 positives, 19 of which were repeated. fter an interval of 1–6 months they gave 9 negative, 9 irritant reactions and ne "non-specific false positive." None of the 19 series of patch tests conformed o the allergic pattern.

Discussion.

The acceptance of erythema alone as evidence of a positive patch test robably accounts for the comparatively high incidence of positive readings. he numerous reactions given to ammoniated mercury, sodium arsenate and otassium iodide indicates that the concentrations used were too high to be mployed as reliable tests of allergy. In a recent publication, Sulzberger (1954) ave 1% as the appropriate strength for testing with sodium arsenate and 5% for potassium iodide; in most cases of true allergic sensitivity positive eactions will probably be given by much lower concentrations than these.

The atopic subject frequently shows a follicular or pustular non-eczematous esponse to patch tests with metals (Sulzberger, 1954). In the present investi-ation atopics gave 15% positives compared with 6·8% in normal subjects, ut most of the 58 reactions given to nickel, arsenic, mercury and dichromate ere of this follicular type. Of the eight patients giving positive reactions to ickel sulphate only one showed clinical evidence of nickel sensitivity. More-ver, to procaine, formalin, paraphenylene diamine, turpentine and pyrethrum he atopic group gave only 7 positives compared with 11 in the group of normal ubjects. There was therefore no evidence to suggest that the atopic patient s by nature any more susceptible to epidermal sensitivity than the normal erson.

The contact dermatitis group gave 50 positive tests to procaine, formalin, araphenylene diamine, turpentine and pyrethrum, a finding which suggests hat many of these patients are polysensitive. When, however, a random eries of six patients originally giving 21 positive reactions was retested in erial dilutions only one test appeared to give a true allergic reaction, the

remaining 20 being most probably false positives. Further work is needed on this subject in order to discover with certainty the proportion of patients with contact dermatitis who are polysensitive.

In patients with either atopic eczema or contact dermatitis, quite strongly positive reactions were often negative on retesting and it would appear that the threshold of reactivity varies not only between normal and eczematous subjects, but in the same individual during different phases of an eczema. The propensity to give false positive reactions may persist for three months after subsidence of the rash. In view of these findings it is considered that, whatever the test substance, a single positive patch test should not be accepted as definite evidence of epidermal sensitivity.

Conclusions.

A series of test substances gave more positive reactions on eczematous subjects than on normals, the highest incidence being in the contact dermatitis group. Most of these reactions are false positives and should not be accepted as proof of epidermal sensitivity.

The threshold of reactivity is inconstant, being lower in the eczematous subject than the normal, and varying according to the phase of the eczema.

Much of this work was done in the Skin Department of the Middlesex Hospital, and I should like to express my thanks to Dr. F. Ray Bettley for his encouragement and advice.

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THROMBOCYTOPENIC SKIN PURPURA FOLLOWING TREATMENT WITH TRINITRIN.

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Thrombocytopenic purpura is known to occur after medication with many rugs. A comprehensive list is given in the full review of Ackroyd (1953), but e have not found a record of a case attributable to nitrites. We recently saw patient in whom the presence of a nitrite thrombocytopenic purpura could be roved.

Case Report.

The patient, a man aged 65, attended for a rash on both legs.

He gave a history of having suffered from hypertension for five years. One year fore seeing us he had had a myocardial infarction and from that time on he took initrin for recurrent attacks of angina of effort. He took up to fifteen 0·5 mg. ablets daily. About 5 months before being seen by us there appeared a symmetrical ash on both lower extremities and buttocks. The rash was composed of patchy, ightly raised, confluent lesions without sharp borders. The lesions were erythe- atous and purpuric, and on applying pressure the erythema faded markedly, and umerous pin-point reddish brown spots remained. Moderate scaling was present ver the tibiae. Itching was pronounced. The question of drug purpura was onsidered.

The blood count showed (per c.mm.): 50,000 platelets; R.B.C. 5·44 million; b 13·5 g.; W.B.C. 5000 (poly. 38%; eos. 4%; lymphos. 48%; monos. 10%); leeding time 2 min. 30 sec. (several examinations); coagulation time 2 min. 20 sec.

General examination.—An obese, stocky man; blood pressure 190/120 mm. Hg; ardiac enlargement; systolic murmur, grade 3, over whole praecordium; palpable ver (4 cm. below costal margin); fundus stage 2; urine, normal.

Capillary microscopy: capillaries appreciably congested, otherwise normal orphology (several examinations).

Histology.—(Skin of thigh) (Dr. F. Sagher): Slight absolute and relative hyper- eratosis was seen and in some places parakeratosis (Fig. 1). The parakeratotic atches were situated over areas of infiltration in the cutis. The epidermis was ightly acanthotic, and here and there passage of cells from the cutis into the epidermis as seen. In the papillary and sub-papillary layer and mid-dermis, small focal nfiltrations were seen around the blood vessels. All the blood vessels in these areas ere dilated, most of them filled with blood and surrounded by red cells, histiocytic ells and some eosinophils. The walls of some of these blood vessels were thickened nd their endothelium swollen. In the deeper dermis there were occasional small nfiltrations of perivascular arrangement. In the vicinity of the sweat glands and

ducts numerous small blood vessels filled with blood were seen. The elastic tissue was lacking in the areas of infiltration but otherwise was normal. Iron stain: negative.

Nitrite medication was stopped and 15 days later his platelets had increased to 180,000 and the purpuric rash had faded markedly. Twenty-nine days after stopping nitrites he took 5 mg. of erythrol tetranitrate for a severe anginal attack. The pain did not abate, so he took a 0·5 mg. tablet of trinitrin. The next morning there was

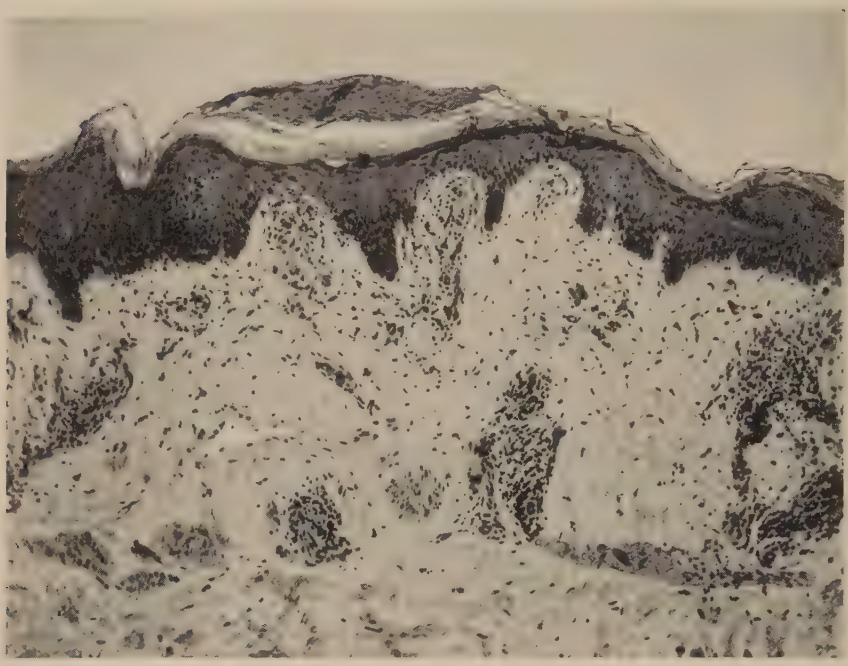

FIG. 1.—Parakeratosis and slight acanthosis over areas of infiltration in the papillary layer. Small foci of perivascular infiltration are seen in the subpapillary layer and mid-dermis.

moderate depression of platelets (of doubtful significance), and the purpuric rash became much more prominent.

> The experiment on the morning of the 30th day of observation was crucial. At 8.30 a.m. there were 132,000 platelets per c.mm. At 11.45 a.m. he was given 0·5 mg. of trinitrin. Three-quarters of an hour later the platelet count was 32,000. By 2 p.m. the platelet count was 182,000; at 2 p.m. 0·5 mg. of trinitrin was again given; 15 minutes later the platelet count was 66,000, and after 1½ hours had reached 208,000. Trinitrin was again stopped.

From 33rd day of observation onwards he took erythrol tetranitrate (at our suggestion) repeatedly for recurrent anginal attacks. There was symptomatic improvement, but the purpura did not return, and there was no appreciable drop in the platelet count. On the 98th day of observation he was stricken with myocardial

nfarction. His platelet count, despite tetranitrate, was 200,000. There was no ash. He died at home two weeks later and there was no autopsy.

Discussion.

The evidence here in favour of trinitrin thrombocytopenia is clear. Stopping rinitrin was followed by the disappearance of the purpura and the return of the platelet count to normal. Taking 0·5 mg. of trinitrin produced marked platelet reduction in 15 minutes and very marked reduction in 45 minutes in two tests. The reduction was temporary.

Administration of quinidine to a patient of Collins (1950) caused almost complete disappearance of platelets from the blood stream in less than an hour. We have under our care a patient with thrombocytopenia due to saridone in whom giving this drug caused marked reduction in platelets and increased bleeding-time within an hour. This rapidity of platelet reduction favours destruction as the reason for the low count, since an interference with platelet production could not produce such prompt results, and on the other hand storage of platelets elsewhere in the body is unlikely. Our patient took trinitrin for seven months before the rash appeared. This is in keeping with the usual story that the offending drug is taken for days or weeks or sometimes for years before untoward results appear.

It is of interest that in our case the bleeding time was not increased, and the patient did not show bleeding from any mucous membrane or viscera apart from the purpuric rash. The possible dissociation of thrombocytopenia from bleeding is well known. The occurrence of a low platelet count in a patient without haemorrhage has been noted repeatedly. It seems that in the present case the thrombocytopenia and purpura were specifically due to trinitrin because the related drug erythrol tetranitrate had no such effect. The formula of trinitrin is $C_3H_5(ONO_2)_3$, and that of erythrol tetranitrate is $C_4H_6(NO_3)_4$.

Very few of the case reports of drug purpura give results of skin biopsy. The result in our patient's biopsy is significant in that blood vessels showed swollen endothelium and much blood was disintegrated outside the capillaries. The blood-vessel pathology in our patient resembles that described by Highstein and Zeligman (1951) in a case of thrombocytopenic purpura due to menthol. Ackroyd stated that apart from this single case report of Highstein and Zeligman, no abnormalities appear to have been noted in the blood vessels in purpura due to drugs. The usual drug purpura shows petechiae set in normal skin without any inflammatory reaction. In our patient there was a confluent rash covering the whole of the lower extremities. It is of interest that in 1943 Davis noted a case of purpura in angina pectoris and another patient with purpura in myocardial infarction; both patients had taken nitrites, but nitrites were not suspected as a possible cause of the purpura.

Summary.

A case of thrombocytopenic skin purpura due to trinitrin is described. Noteworthy features of this case are normal bleeding-time, the absence of bleeding from mucous membrane and viscera other than the skin, and the presence in skin biopsy of blood vessels with swollen endothelium. Although trinitrin caused thrombocytopenia and skin purpura in this patient, erythrol tetranitrate did not.

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IDIOCY AND ECTODERMAL DYSPLASIA.

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The majority of mental defectives in England and Wales are above imbecile level (O'Connor and Tizard, 1954). Most of these feeble-minded persons are not obviously different in appearance from normal citizens and are not readily classifiable into clinical entities. Among the idiots and imbeciles, on the other hand, there are many who look grossly abnormal and who can be so classified. This is particularly so where the mental and associated somatic defect has been determined by an early embryopathy. In some of these cases environmental factors are important, e.g. rubella ; in other cases there is a presumption of hereditary factors, e.g. familial inherited cataract. Many such dystrophies do not fit readily into any of the recognized syndromes which often overlap and blend. There are also a number of syndromes which are sometimes associated with mental deficiency, such as Apert's syndrome, but which also occur in persons of normal intelligence. However, it remains useful to attempt to recognize and describe defined syndromes amongst children with gross dysfunction of the nervous system since to do so may give a clue both as to the stage in embryonic or later life at which the damage was done and to the aetiology.

A case of anidrotic ectodermal dysplasia is described here.

Case History.

The patient is the fifth of six children. All the others are normal. The father, a petty officer in the Royal Navy, was killed during the war. The mother was a domestic servant prior to marriage. A maternal uncle suffered from epilepsy and confusion. After treatment in a mental hospital with mesantoin he returned to work. He had no cataract or other evidence of ectodermal dysplasia. He did not suffer from loss of hair or hypogenitalism and was not regarded as mentally defective. A paternal uncle attended a school for the educationally sub-normal and was subsequently in a colony for rehabilitation but was not, apparently, a case of ectodermal dysplasia.

The patient was born without difficulty in hospital, the mother having been well during the pregnancy. However, she took 3 boxes of " Ladies Relief Pills " in the first two months of pregnancy with a view to abortion. She attempted abortion with none of her other children.

At birth the baby weighed $8\frac{3}{4}$ pounds but was noted to be delicate and deformed. There was no jaundice. The child failed to progress. She never walked, talked, acquired clean habits or saw. Desquamation of hands, feet and the top of the scalp were noted soon after birth. She was admitted to the Fountain Hospital at the age of $2\frac{1}{2}$. She was then almost devoid of hair. The head circumference was $18\frac{3}{8}$ inches. The nails were vestigial. The skin of the hands, feet and nose was atrophic and scaly.

She gurgled but had no speech and did not respond to speech. She had no interest in toys. She was spoon fed.

Present condition : She is a vegetative idiot, now aged 18. She is blind with bilateral cataract. She turns her head towards sounds. She has a grasp reflex but does not use her hands. She cannot stand or walk. She is without speech and is doubly incontinent. She is assessed on the Vineland scale as having a " developmental age " of four months. She is spoon fed with soft food. She shows no interest in her surroundings and makes no rapport.

Physically she presents the usual dysplastic picture of the crippled idiot, weighing now at the age of 18 only 4 stone and 5 pounds. She has the poor peripheral circulation and musculature usual in these cases. In addition she is completely bald except for a small wisp of hair in the centre of the head. There is no hair elsewhere on the body. She has no eyebrows, eyelashes, axillary or vulval hair. The nails are almost absent from both fingers and toes, being represented only by a thin soft, membrane on the first and second digits (Figs. 1 and 2). The skin is very fine, thin and shiny with some desquamation over the hands, feet and top of the head. The teeth are normally developed except that the third molars are absent. The breasts have reached an 11-year-old stage of development. No nipple is obvious though there is an areola. The vulva is at a pre-pubertal stage of development. No menstruation has taken place. Sounds are occasionally emitted in a gruff voice. The plantar responses are extensor. The blood pressure is 120/75.

Heating for one hour with an electric pad under the blankets produced no appreciable sweating. The skin remained quite dry although the patient was very hot, flushed and obviously rather uncomfortable.

Further testing with quinizarin after the administration of 10 grains of aspirin by mouth and comparison with another patient showed that the anidrosis, although not complete, was almost so. Only very slight blue discoloration of the powder was produced in localized areas. After application of an electric heating pad for one hour the patient's temperature was, however, no higher than that of the control.

The urine showed no abnormality. The test for phenylpyruvic acid was negative.

Blood Groups :—	ABO	Rh.	MN	S	P	Lewis	Kell	Lutheran
	0	rr	N	Neg.	+	Neg.	Neg.	+

Blood cholesterol 208 mg./100 ml.

Skiagram of the skull normal.

The toxoplasmin skin test was negative but she was positive to 1/10,000 tuberculin.

The electroencephalogram (Dr. D. A. Pond) showed normal widespread symmetrical patterns of fast and slow activity.

Comment.

Classifications based on germinal layers have a very limited value in clinical practice since in many conditions more than one layer is directly involved, e.g. in tuberose sclerosis. The present case can, however, be regarded as largely ectodermal and can be placed in the anidrotic group. It is clear that such a gross dysplasia, with absence of the sweat glands and hair follicles, coupled with defective development of the lens and of the brain must have been determined during the first few months of intra-uterine life.

Anidrotic ectodermal dysplasia is usually looked upon as an hereditary anomaly (Sorsby, 1953). The present case differs from others which have been described.

The teeth are well formed and the lower jaw is normal in contrast to the usual finding of deformed or absent teeth and under-development of the lower jaw. Moreover, the mammary glands are not only present but have achieved a considerable degree of development. Most of the described cases have been males and the condition is considered to be sex-linked to males with females showing minor disorders, such as absence of canines. Affected individuals have usually been of normal intelligence, though diminution of intellectual capacity to the level of feeblemindedness has been recorded (Penrose, 1954). A great variety of similar syndromes have been described and the distinction between them is not sharp. For example, this case shows many of the features of dystrophia myotonica except that there is no myotonia.

Fig. 1.

Fig. 2.

Much emphasis has been placed in the past half-century on genetic factors in mental defect. More recently the discovery of the role of maternal rubella and other factors has restored interest in the role of the environment. Little is known about the effect of abortifacients in producing embryopathy. A great many attempts at chemical abortion are made and a high proportion of these are unsuccessful. There has been some tightening up of the regulations governing the sale of abortifacients since the case reported here was born. At that time pills containing apiol, ergot or quinine were freely sold for this purpose. In view of the large dose taken and the fact that the patient's dystrophy does not fit into any of the recognized hereditary categories it is impossible to dismiss the possibility that the abnormality is due to the toxic action of one or more abortifacients.

A study of attempted abortion in relation to mental deficiency would be useful though the task is beset with obvious difficulties since, naturally enough, few women who have made such an attempt are prepared to discuss the matter frankly. On the other hand many mothers who have a mentally defective child after taking a draught of some innocuous substance in the hope of procuring an abortion are subsequently burdened with feelings of guilt, although it may be possible to demonstrate conclusively that the defect is due to some totally different cause.

Summary.

A case of anidrotic ectodermal dysplasia in a girl of 18 is reported. It was unusual in that the patient is female, an idiot, has good teeth and jaw development and has fairly well developed breasts. There is no family history of the condition. The mother took two boxes of "Ladies' Relief Pills" early in pregnancy. The possibility that these were responsible for the defect is discussed.

I wish to thank Mr. R. Warner Weir for reporting on the dental condition.

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ACRODERMATITIS PUSTULOSA HIEMALIS: REPORT OF TWO CASES.

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Papulo-necrotic tuberculides are one of the common varieties of tuberculide. The lesions may localize themselves to the face as "acnitis", or the deep form of papulo-necrotic tuberculide; or limit themselves to the dorsa of hands and feet, as "folliclis" or the superficial type of tuberculosis papulo-necrotica; or they may affect other areas and comprise other varieties.

The essential lesion in papulo-necrotic tuberculide is a small intradermal erythematous papule which may be surrounded by an erythematous zone. As the lesion slowly increases in size the colour darkens from red to a deeper blue and finally a vesico-papule or a vesico-pustule is formed in the course of a few weeks. The lesions tend to be grouped and vesico-papules, pustules, or nodules may be present. On palpation the lesions are firm and painless. They may occur in crops every few months, followed by recurrences, and the attacks may continue for years.

More than one variety of papulo-necrotic tuberculide may occur together, or in association with other tuberculous manifestations.

In folliclis, the lesions tend to be more superficial, appearing first as painless red macules, and over a period of 4 to 6 weeks they develop into firm papules, vesicles, or pustules. Finally such lesions dry up, crusts form which may be depressed at the centre and ultimately they involute, leaving a small scar. The eruption may recur after healing, and this may extend for a long time, even for years. The sites commonly involved in folliclis are the hands and feet, especially their dorsal aspects, forearms, legs and ankles; the trunk is seldom affected. Lesions on the fingers tend to be more indolent.

A disorder very similar, if not identical with folliclis, was described under the title "Acrodermatitis pustulusa hiemalis" by Radcliffe-Crocker. His description taken from three cases was as follows: "The lesions are all excited or kept up by cold, affect the hands only, especially about the knuckles and sides of the fingers, and take the form of indolent indurated papulo-pustules, isolated and few in number at a time; but the disease as a whole persists by a succession of lesions throughout the winter and early spring. They begin as hard, brown, large pin's-head points, but later as if there was a "thorn in the flesh"; if pricked early, watery fluid issues, but later matter forms round the peg, and the whole is on a red raised base the size of a large pea. The central portion comes

way and leaves a hole which heals very slowly and leaves a scar. A few form ndurated red nodules without suppuration."

Case Reports.

I observed two typical cases of acrodermatitis pustulosa heimalis during January nd February 1954, and demonstrated them before the Egyptian Dermatological and enereal Society during the meeting at Dar El Hekma, in February 1954.

Case 1.—A boy aged 14 years, a student in a secondary school, having 6 brothers nd sisters, mother and father, all leading a normal life.

His illness began 3 years previously, and lasts during each winter, beginning about ecember and ending by the end of March or the beginning of April.

Fig. 1.

The lesions are limited to the dorsa of both hands, particularly the knuckles and ides of the fingers (Fig. 1). The lesions are mainly papulo-pustules with necrotizing epressed centres, but some nodules are also present. They are firm, painless, dusky ed in colour, with areas of necrosis, crusting, and slightly depressed small scars of revious lesions. Some of the lesions tend to be grouped, especially about the knuckles f the left hand. Enlarged tuberculous lymph glands were found on both sides of he neck, more marked on the left side. The larger of these glands was a group just elow and posterior to the angle of the left mandible, and gave rise to a visible swelling. here was no other clinical evidence of tuberculosis, and lungs were normal.

Urine and stool examinations were normal.

Tuberculin test was positive in a concentration of 1/10,000. Biopsy revealed uberculous aggregations.

W.R. was negative.

Case 2.—A girl aged 15 years had the lesions on both hands and the lower parts f both forearms recurring every winter for the last four years.

The patient has an intractable cough. Chest skiagram showed increased hilar hadows, considered to be due to enlarged tubercular lymph nodes.

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INCONTINENTIA PIGMENTI.

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Case Report.

A Hindu male child 7 months of age was brought to me in January 1952 because of pigmentation all over the body.

History.—The baby was the full-term second child of a healthy mother who had had an uneventful pregnancy, confinement and puerperium. The parents had no history of skin disease or of syphilis. The brother of the patient was 5 years of age and was healthy with no skin disease. The child's head was very large at birth and was growing larger. The child was delivered in a nursing home in Calcutta and from the notes it appeared that he developed a morbilliform erythematous rash all over the body about 24 hours after birth. There was no rise in temperature. The rash subsided in about 10 days, leaving macular blackish pigmentation all over the body. The colour of the pigmentation had since deepened. The baby was never seen to scratch the skin.

On examination the child was found to be under-developed and ill-nourished, with hydrocephalus and patchy alopecia. At 7 months of age the child could not sit unsupported. The eyes were sunken with bulging fontanelles and prominent temporal veins. There was very little subcutaneous fat, the skin was hyperelastic and the patient could easily have been passed as a case of Ehlers-Danlos syndrome. The nails were ill-developed and were pigmented brown. The skin of the whole body except the face presented chocolate coloration and at places slaty coloured whorls, spider-like figures. Bizarre figures covered the whole trunk, particularly the flanks. Slaty linear and bizarre figures were present on all the limbs. The lesions were macular and were not itchy (Fig. 1).

The typical slaty pigmented bizarre macular lesions with hydrocephalus, patchy alopecia, dystrophic nails and the history of an erythematous morbilliform rash made up a typical picture of incontinentia pigmenti.

The patient was given vitamin C, 100 mg. by intra-muscular injection twice daily for a week, followed by 50 mg. every 8 hours by mouth for a long time. When seen in 1955 the child was about 4 years old and at this time one could hardly see the pigmented bizarre figures on the skin. None of the teeth had erupted and the nails presented a discoloured appearance with deformation. The child was otherwise normal.

The parents did not agree to biopsy. However, the pigmentation was so typical with the characteristic bizarre appearance associated with ill-developed nails of fingers and toes and hydrocephalus with soft, brittle hairs and patchy alopecia, that the diagnosis of incontinentia pigmenti was not difficult.

When last seen in July, 1955, at the age of 4 years, the pigmentation still shows the bizarre appearance though the colour has faded. The hydrocephalic head shows several prominent veins on the temporal regions, the eyes are sunken and there is patchy baldness ; nail lesions present the typical picture of pachyonychia congenita.

The patient was again treated with 200 mg. of vitamin C daily by injection for 2 weeks and 50 mg. twice daily by mouth for 3 months. The child was treated also

th local application of hydrocortisone ointment twice daily for two weeks and ce daily for 6 weeks resulting in complete fading of the pigmentation.

Discussion.

This is the first case of incontinentia pigmenti reported from India; 21 ses have been reported from Japan and together with this form 22 cases from e whole of Asia.

Several dermatologists in different countries of the world have observed fferent signs and symptoms and varied types of cutaneous lesions, but all

Fig. 1.

gree that incontinentia pigmenti usually commences during the first few eeks of life and is preceded by a morbilliform rash which may be regarded the initial inflammatory stage. Another type of the disorder has been escribed where this initial inflammatory stage is absent and the disease mmences as late as at 2 years of age. Franceschetti and Jadassohn (1954) ave distinguished two different groups on the basis of signs and symptoms ported in the literature from different countries. The first group or the ulzberger-Bloch type occurs almost exclusively in females with splash-like igmentation and absence of malformations. The second group or Naegeli pe affects both sexes with reticular pigmentation and various malformations.

Incontinentia pigmenti is said to be a rare disease in the United States of merica (Ormsby and Montgomery, 1954). Cases have been reported from lmost all parts of Europe, but from Asia it has hitherto been reported only rom Japan. The cause is not known. Haber (1952) suggested that it may

be produced by some virus infection of the mother during pregnancy, but in the case reported here there was no history to suggest this. Incontinentia pigmenti has been said to be caused by the inability of the basal cells to hold and metabolize melanin pigment (Siemens, 1929 ; Sulzberger, 1928 ; Kalz and Mackenzie, 1947). Naegeli (1927) thinks it to be a familial chromatophore naevus. I wonder if it could be due to some inherent inability to utilize vitamin A, causing higher vitaminosis A and deficiency of vitamin C, since both help pigment formation.

It is thought to be of an hereditary nature (Allan, 1954) and has occasionally been observed in two members of a family (Dowling and Whitlock, 1952). Incontinentia pigmenti has practically always been observed to be associated with ectodermal defects, such as dystrophy of nails, ocular troubles, absence or malformation of teeth, alopecia, paralysis, epilepsy and mental deficiency (Ormsby and Montgomery, 1948 ; Franceschetti and Jadassohn, 1954 ; Kitamura *et al.*, 1954).

The initial lesion is commonly morbilliform and inflammatory in character, as in the case reported here. Carney (1951) has pointed out that about half the patients exhibit an inflammatory infiltration, about 30% present bullae and vesiculation as an early symptom, and in about a third of the total number of patients the lesions are warty. Early vesicular lesions were found to be quite common by Lewis (1954). Moynahan (1954) observed generalized exfoliation at birth of a female child which cleared with local treatment and was followed by the appearance, after a month, of lichen planus-like lesions on chest, axillae and face, which faded away soon, leaving brown pigmentation with bizarre pigmented striae ; the child's mother had the same for the first 10 years of her life and cleared up spontaneously.

Summary.

The first case of incontinentia pigmenti reported from India making a total reported cases of 22 from Asia.

Vitamin C and cortisone form the sheet-anchor of treatment.

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Dowling, G. B. and Whitlock, F. A. (1952) *Practitioner,* **168**, 453.
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Siemens, H. W. (1929) *Arch. Derm. Syph., Berlin,* **157**, 382.
Sulzberger, M. B. (1928) *Ibid.,* **154**, 19.

NORTH BRITISH DERMATOLOGICAL SOCIETY.

Edinburgh, 9 December 1954.

Reaction to Cinnabar in a Tattoo.—Dr. Alan Lyell.

A miner, aged 27, was tattoed 13 years ago in red and blue without any local reaction. The tattoo gave no trouble until 3 months ago, when the red areas became acutely inflamed and painful and proceeded to slough and then heal, leaving depressed scars. The blue areas were unaffected. A multiform toxic erythema accompanied the acute stage.

Comment.—The red tattooing is presumably done with cinnabar—a compound of mercury. The patient has not been exposed to any mercury compound as far as he knows (pill, mixture, ointment, lotion, powder, purgative or tooth filling). It was suggested that fulminate of mercury used in detonators could have been responsible.

Eleven other cases also were shown.

Aberdeen, June 1954.

Case for Diagnosis: ? Reticulosis.—Dr. T. E. Anderson (for Dr. J. A. McConachie).

A woman aged 73.

History.—The condition began as a widespread eruption on the trunk and limbs five years ago, spreading to involve the face over two years ago. At first there was mild itching of the arms and legs, with a burning sensation, but subjective symptoms disappeared with the development of the eruption.

Examination.—Large, raised, erythematous, infiltrated plaques of vertex, forehead, cheeks, chin and back of neck, with a brownish-yellow tinge. Similar lesions are present on the arms and forearms, with considerable brown pigmentation and some scaling. On the extensor aspect of the left elbow an infiltrated plaque is ulcerated; biopsy of this lesion revealed a squamous epithelioma, which was treated with a radium mould. The trunk and lower extremities, particularly the latter, showed widespread smaller lesions of lupoid appearance, with marked deep brown pigmentation in older resolving lesions.

Investigations.—ESR (Westergren) 15 mm. in 1 hr. Wassermann reaction, Kahn test, Mantoux test (1/10,000 up to 1/100), Kveim test, skiagrams of chest and phalanges—all negative. Blood count showed a slight hypochromic anaemia, with normal white cells. Serum cholesterol—210 mg.%.

Histology.—Numerous biopsies showed a granulomatous reaction in the dermis, composed of histiocytes, lymphocytes, a few plasma cells and polymorphs, but no eosinophils. There was a slight tendency to follicle formation and in one biopsy several histiocytic giant cells were found.

Treatment.—Treatment with Isoniazid and later with ACTH has produced no material improvement in the condition. The left elbow remained well healed after irradiation.

Postscript.—A test dose of 250r of x-rays was given on 11.vi.54, as suggested by several members, to a 3 cm. circle field on the face, but no appreciable change took place within six weeks other than a very slight involution of the eruption in all areas equally.

Recurrent Acute Dermatomyositis. Dr. I. Caldwell.

A boy aged 15.

History.—On 26.xi.51 following a throat infection this boy was admitted to hospital with a violently acute illness characterized by high continued fever (102–104° F.), a pleomorphic erythematous skin eruption, gross peritonsillar necrosis, and periorbital oedema with heliotrope lids; erythema and oedema over muscle groups of extremities and back, which at first showed brawny induration, tenderness and extreme pain on movement and later gross generalized atrophy ; and leucocytosis, which rose gradually to 122,500/c.mm. and creatinuria of 840 mg./24 hours. High daily dosage of cortisone failed to control this outburst and had to be discontinued on account of a rising blood pressure and painful fluid retention. His illness continued unabated for four weeks and the patient appeared to be almost moribund when 3-hydroxy-2-phenyl cinchoninic acid (H.P.C.) 1 g. daily was commenced and a dramatic response of pyrexia and general condition followed within 24 hours.

Within a few weeks the patient became convalescent and ambulant, and muscle power and bulk slowly returned. After six months the only residua of this attack were a faint branny desquamation of the face, striae distensae of both calves and popliteal fossae and mummification of the terminal phalanx of the right 5th finger.

On 4.ii.54 for the first time since his illness he developed a sore throat, which was treated with one of the sulphonamides for 3 or 4 days before he returned to work. On 11.ii.54 he began an explosive replica of his first illness (T. 104–105° F.), necrotic throat, orbital oedema, pleomorphic cutaneous lesions ranging from erythema nodosum to erythema multiforme and nodular vasculitis-like lesions of his fingers and toes. Muscle symptoms and signs followed the previous pattern and white blood cells reached 74,000/c.mm. On this occasion H.P.C. 1–2 g. daily did not produce any dramatic response but may have tided him through a fulminating phase of the illness.

Examination..—He now shows that muscle power and bulk are rapidly returning with some persistent clumsiness and weakness of his leg muscles. The original residua of his first attack have been augmented by mummification of the tip of the left index finger.

Comment.—A search of the literature has revealed only one reported case of recurrent dermatomyositis (Holmes, 1948).

Although these episodes are compatible with the diagnosis of acute dermatomyositis the possibility of polyarteritis nodosa is not excluded and it may be that the administration of sulphonamide tablets prior to the second attack is of aetiological significance.

Reference.

Holmes, J. McD. (1948) *Brit. med. J.*, **2**, 511.

Sjögren's Syndrome.—Dr. T. E. Anderson.

A woman aged 62.

History.—In 1951, following nervous prostration on the death of her husband, she began to suffer from extreme dryness of the mouth and eyes and a few months later she noticed a slowly progressive, painless enlargement of both parotid glands.

Examination (September 1953).—Bilateral parotid enlargement. Extreme dryness of the mouth with painful fissuring of the tongue. Absence of lacrimation. A periarticular swelling of the right ankle.

Investigations.—Blood count normal. Fractional test meal normal. Schirmer's tests (both eyes) : almost complete absence of moisture. Fluorescein : corneal ulceration present in the left eye.

Histology.—Parotid section is compatible with the diagnosis of Sjögren's syndrome (Morgan and Raven, 1952) : A dense lymphocytic infiltration of parenchyma with small isolated functioning islets of secretory tissue.

Surgical occlusion of the tear duct puncta was performed by diathermy to conserve ears, with considerable symptomatic relief to the eyes. In October 1953, ACTH 5 mg. daily with gradual reduction was given with excellent temporary relief—complete reduction of the parotid swellings, increase in salivation and return of the tongue to normal. This remission lasted for 2 or 3 months and then enlargement of the glands and dryness of mouth and eyes re-appeared. A second course of ACTH commenced 10 days ago has resulted in a similar remission.

References.

Morgan, A. D. and Raven, R. W. (1952) *Brit. J. Surg.*, **40**, 154.

Epidermolysis Bullosa Simplex with Tylosis Plantaris.—Dr. I. Caldwell.

A girl aged 6.

History.—Recurrent bullous lesions particularly of hands and feet but also occurring round the mouth, neck and genito-crural region. There is considerable itching, which has been more severe in summer.

Family history.—Paternal great-grandmother had blisters on her skin. Father had skin disease of unknown type.

Examination.—(6.vi.51) Bullous purulent and haemorrhagic lesions distributed as above with well-marked grouping and some with serpiginous outlines. At first they suggested juvenile dermatitis herpetiformis, but treatment with sulphapyridine was ineffective.

Histology.—Sections show intra-epidermal bullae with scanty cellular infiltrate in the dermis, mainly of lymphocytes and occasional polymorphs.

During the following year follicular hyperkeratotic lesions appeared on the back and limbs and irregular hyperkeratosis developed on both soles.

At present bullous lesions continue to develop, especially on the hands and feet, well-marked tylosis plantaris is present and follicular hyperkeratoses are present on the upper arms. No scarring, atrophy or milia formation has occurred.

This case appears to correspond to some extent to those described by Everall (1954) who suggested they might be a variant of epidermolysis bullosa simplex with pressure as factor in production both of bullae and of tylosis. The resemblance of other cases to juvenile dermatitis herpetiformis was mentioned by Dowling and Meara (1954), who proposed however to include them in the congenital epidermolysis bullosa group.

References.

Everall, J. (1954) *Brit. J. Derm.*, **66**, 54.
Dowling, G. B. and Meara, R. H. (1954) *Ibid.*, **66**, 139.

Pyoderma Gangrenosum. Dr. I. Caldwell.

A woman aged 42.

History.—Recurrent attacks of ulcerative colitis since 1948 with short remissions lasting no more than three months. For the past eighteen months extensive lesions of pyoderma gangrenosum have been present on the left thigh, left hand, chest, face and back. Injections of penicillin have been incriminated as determining the site of origin of fresh lesions.

Investigations.—Culture from ulcer: *Staph. aureus* and *Ps. aeruginosa*. Stools: macroscopic blood, mucus and epithelial debris. Barium enema: Loss of haustration in the descending and sigmoid colon.

Histology.—Acute inflammatory changes.

The patient continued a non-remitting febrile course (T. 100–102° F.) and showed little response to local or parenteral antibiotics. Three loose motions per day were passed.

With the intention of improving her condition sufficiently to make a colectomy feasible, cortisone 100 mg. daily was started on 10.v.54. Within six hours her temperature fell to normal and remained so ; within three days her bowel symptoms cleared and stools became virtually normal, and within the next fortnight her skin lesions began to heal rapidly. The skin ulcers now show complete central healing with a thin peripheral rim of ulceration not yet healed. Cortisone dosage is being slowly reduced at present.

The following cases also were shown :

Lichen Sclerosus et Atrophicus; Lupus Erythematosus (2); Sarcoidosis.—Dr. T. E. Anderson.

Sarcoidosis; Dermatomyositis (2).—Dr. I. Caldwell.

Alopecia and Myxoedema.—Dr. W. T. Hendry.

Lichen Planopilaris.—Dr. H. Edwards.

NORTH OF ENGLAND DERMATOLOGICAL SOCIETY.

Leeds, 8 March 1955.

Naevus of Ota.—Dr. Clifford Stuart.

A man aged 24.

History.—He was hit by a cricket ball below the right eye three years ago. The swelling subsided but pigmentation remained. He has never used eye drops.

Family history.—There is no history of this condition in the family. His parents are of English descent.

On examination.—There is a flat brownish-black area of pigmentation below and to the right of the right eye, affecting an area 7 cm. by 3 cm. There is no pigmentation of the sclera.

Histology (Dr. H. Haber).—The section represents probably an aberrant Mongolian spot known also under the name of naevus fuscocaeruleus ophthalmo-maxillaris (Ota).

Comment.—According to Dorsey and Montgomery (1954) the naevus of Ota is essentially a Mongolian spot located on the side of the face and involving the eye. Many cases have been described, several being first noticed in the third decade. Cornell (1937) reported a probable case involving the sclera which spread to the skin following an injury.

References.

Dorsey, C. S. and Montgomery, H. (1954) *J. invest Derm.*, **22**, 225.
Cornell, A. H. (1937) *Arch. Derm. Syph., Chicago*, **36**, 1261.

Pretibial Myxoedema.—Dr. S. T. Anning.

A nulliparous canteen assistant, aged 46, complains of aching of the legs and thickening of the skin over the shins; it has been present for one year in the left leg following a slight knock, and for one week in the right.

Previous history.—No history of any disease of the thyroid. Seven years ago she had an attack of pneumonia with pleurisy, before which she had been very tolerant of cold weather, and had lost weight. After this attack she gained weight. Four months ago she noticed a little prominence of her eyes, but there was no diplopia. She now prefers hot to cold weather.

Family history.—Nothing relevant.

Examination.—Sallow, rather pallid complexion and a slightly husky voice. Moderate proptosis (3 mm. right, 6·5 mm. left). Eye movements full with no muscular weakness. The thyroid feels small and shrunken.

Over the anterolateral aspect of the lower thirds of both legs are thickened areas (7 × 7 cm. on the right, and 14 × 10 cm. on the left), skin coloured or slightly erythematous with a coarse dimpled surface. The skin generally is a little dry with sparse eyebrows and the hair otherwise fine though not particularly thin.

Blood pressure 125/90 mm. Hg. General examination otherwise normal.

Investigations.—Hb 83%. Blood count: RBC 4·0 mill./c.mm. WBC 6000/c.mm. (Neutros. 48%, lymphos. 51%) ESR normal. Blood cholesterol 0·21%. Skiagram of chest and skull normal.

B.M.R. normal on two occasions.

Histology.—The specimen was placed in formalin solution and staining for mucin was negative. The appearances otherwise were consistent with those of pre-tibial myxoedema.

Comment.—This patient has pre-tibial myxoedema with proptosis but no history of thyroid disease; however, symptoms suggestive of mild hyperthyroidism changed to those of hypothyroidism after pneumonia. It may be that necrosis of the thyroid occurred during that illness.

Local treatment of the left leg with hydrocortisone cream (2·5%) three times a day for two weeks had a little temporary effect, the area becoming slightly softer. In consultation with Prof. Hartfall it was not thought wise to use cortisone internally. The patient is now being treated with L-thyroxine sodium, 0·05 mg. twice daily.

Localized Dermatitis Herpetiformis.—Dr. F. F. Hellier.

A man aged 55.

History.—For 10 years he has had recurring blisters under the chin spreading up on either side of the neck towards the ears. The longest free periods have not been more than two months and he has never had any skin lesions elsewhere. Treatment for " chronic impetigo " has been quite unsuccessful.

When seen at the out-patient department there was a red crusted area spreading in a band under the chin with one largish unruptured blister. There were no lesions elsewhere except for a crusted spot on the front of the scalp. The vesicle fluid was sterile on culture.

Histology.—The blister was situated sub-epidermally.

Under treatment with diamino-diphenyl sulphone, 50 mg. twice daily, the blisters ceased, but relapsed five days after it was stopped, clearing again on restarting the drug.

Comment.—When I first saw this man I diagnosed Hailey-Hailey disease. However, histological investigation and later the response to DADPS suggested the diagnosis of dermatitis herpetiformis. The possibility of a localized form was suggested to me by the report by Costa and Gontijo (1954) of a girl who had lesions of dermatitis herpetiformis limited to the legs for 5 years.

Reference.

Costa, O. G. and Gontijo, J. (1954) *Ann. Derm. Syph.*, **81**, 528.

CAT.

OBITUARY.

PROFESSOR LEOPOLD ARZT.

On the 20 May 1955 the former Principal of the Department of Dermatology and Syphilology in Vienna, Professor Leopold Arzt, died in his seventy-third year shortly after he had suffered a stroke.

Following on the demise of Riehl, his chief, Arzt took over Hebra's clinic in 1926 and directed it until 1938 and then from 1945 until he became Emeritus in 1954.

He was universally recognized as an outstanding physician, specially appreciated as an academic teacher for his didactic talents and well known by his dermatological colleagues throughout the world as a scientist and research worker. His published work includes 300 papers dealing with all branches of dermatology and venereology ; special mention may be made of his contributions on mycosis fungoides, on Hodgkin's disease and leukaemia of the skin, on microsporosis and other mycoses, on burns, occupational dermatoses, xanthomatoses and tularaemia. He made numerous contributions on radium therapy of skin cancer and researches on syphilis.

Arzt distinguished himself in dissertations at numerous dermatological congresses and meetings all over Europe and the United States by his exact morphologico-clinical approach. Latterly he was specially welcomed at the International Dermatological Congress of London in 1952.

His far-reaching knowledge and his meritorious achievements were universally recognized. He was corresponding and honorary member of numerous medical societies all over the world, and Honorary Foreign Member of the British Association of Dermatology since 1936.

Medicine in Vienna has lost in Arzt one of its greatest masters ; his memory will serve as shining example for posterity.

A. M.

Dr. PHILIP BURNETT.

Canadian Medicine suffered the loss of one of its senior dermatologists in the death of Philip Burnett, D.S.O., M.A., M.D., C.M., M.R.C.P., F.R.C.S., who died in Montreal on 18 March at the age of 77 years.

A Montrealer by birth, Dr. Burnett early renewed the ties of his Old Country heritage by attending Clifton College in England. After his graduation from the Arts Faculty at McGill University he completed his medical course in 1900, later to serve his internship in Montreal General Hospital.

Returning to Great Britain, he was fortunate to have as his mentor Dr. J. M. H. MacLeod, who directed his steps into a specialty scarcely then trodden by Canadians. Dr. MacLeod, Dr. Galloway, Sir Norman Walker and Sir Malcolm Morris contributed much to his formative years, and the life-long friendship he formed with MacLeod was only terminated by the death of his old chief. Brocq, Darier, Sabauraud and Gaucher moulded his dermatological thought during his studies in Paris. Unna and Joseph greatly aided him while he sojourned in Germany, and he constantly recalled the fruitful days spent with Neisser in Breslau. Further work done under Ehrmann and Riehl with other professors in Vienna brought back to him in later years memories of happy days in that, then, carefree country.

CAT.

During the Great War Dr. Burnett served in the Canadian Expeditionary Force in England and France. While in France he was consultant in dermatology to the Canadian Corps ; he was awarded the Distinguished Service Order for outstanding services and devotion to duty while under fire during the Battle of the Somme.

Dr. Burnett established the first skin clinic in the Royal Victoria Hospital, Montreal, in 1904. At the time of his retirement from McGill University and from the hospital in 1942, he held the positions of Clinical Professor of Dermatology and Dermatologist-in-Charge of Service. In 1945 he was appointed to the Honorary Attending Staff of the hospital. His service spanned a period of nearly forty years and during that time he instructed successive generations of McGill medical students in the art of clinical dermatology. The forceful style of his teaching was tempered with many touches of humour. His Old Country training was reflected in his appraisal of his diagnostic problems ; all component elements were recognized and added up to the sum of a correct diagnosis of the presenting problem.

Dr. Burnett made but few contributions to the literature, but gave freely from his vast store of clinical experience to his students, interns and staff. He was a modest, unassuming man, punctual in his medical assignment and kindly to those who were tardy with their duties. The indigent sick and children patients received his special attention.

He was a man's man. An athlete in his younger days, an out-of-doors enthusiast and a gentleman farmer, he was one who was thoroughly at home with rod or gun in the Laurentian woods. He was beloved by his English-Canadian and French-Canadian confrères.

With Dr. King Smith of Toronto, Dr. Omar Wilson of Ottawa, Dr. Bedford of Winnipeg, and Dr. Fred Burgess of Montreal, he was instrumental in forming the British Association of Dermatology Canadian Branch in 1927 and was later elected an honorary member. He was a founder member of the Montreal Dermatological Society and was elected its first president in 1930-31. Dr. Burnett lived to see the specialty which he had pioneered in Montreal rise to a high place in Canadian medicine. The wisdom and fatherly touch of the Chief will be sorely missed by all of us.

L. P. E.

Dr. GEORGE MacKEE.

George Miller MacKee (1878–1955) began his dermatological career in 1904 when he became associated with Dr. Fordyce who was then Professor of Dermatology and Syphilology at the New York University and Bellevue Hospital Medical College. Six years later, Fordyce became Professor at the College of Physicians and Surgeons, Columbia University, and Dr. MacKee served there in various academic positions. He became Professor in 1927 and continued in that capacity until 1933. In 1934 Dr. MacKee was appointed Professor of Clinical Dermatology and Syphilology and Executive Director of the New York Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He held this position until he reached the age of retirement and was then made Professor Emeritus of Dermatology, being succeeded by Dr. Marion Sulzberger.

Throughout Dr. MacKee's long and productive career he was accorded practically all the honours as well as the responsibilities of the specialty. His major interest was the training of young men and women in dermatology and he really devoted his entire time and effort to such training and to organizing teaching facilities and financing scholarships for many years.

Dr. MacKee was a pioneer in dermatological roentgen therapy. His paper on "Arithmetical Computation of Roentgen Dosage" in 1919 was a classic for at least two decades. A notable achievement was his book, *X-rays and Radium in the Treatment of Diseases of the Skin*, the last and fourth edition of which was written in collaboration with Dr. Cipollaro.

For many years Dr. MacKee was Editor of the *Journal of Cutaneous Diseases* (1908–1918) and subsequently was on the editorial board of the *Archives of Dermatology and Syphilology* until recently. He published a multitude of original papers on a wide variety of dermatological subjects, the best known being purpura annularis telangiectodes, monilethrix, Kaposi's sarcoma, neurotic excoriations, congenital ectodermal defect, and many articles on the radiotherapy of skin diseases.

G.C.A.

BOOK REVIEWS.

Viral and Rickettsial Diseases.*

This excellent book makes an immediate appeal to the dermatologist because it presents a lucid and critical summary of our knowledge to date concerning the viral and rickettsial diseases which primarily or secondarily affect the skin and mucous membranes. The subject is introduced by a discussion on the nature of viruses and their intracellular development, and here it is interesting to note the phenomenon of "lysogeny" which may explain some of the anomalies of herpetic infections.

In Chapter 2 are described the laboratory techniques by which the clinical diagnosis of virus diseases may be established, and so concisely is this done that it does not mar the predominantly clinical presentation of the work as a whole.

Herpes simplex is adequately described, but one is surprised to find a decided bias in favour of psychotherapy in authors who are so well informed of the organic basis of viral diseases. The irrational method of treating recurrent herpes by repeated vaccination with vaccinia lymph is mentioned and rightly discredited, but no mention is made of trying to raise the specific antibody level by vaccinating a subject with autogenous herpetic vesicular fluid or by the use of formalized herpes vaccine. Probably such treatment would be more troublesome than the disease, but at least it is rational.

The authors support the monistic view of chicken-pox and zoster and their review of the abundant evidence should remove all doubts: this also applies to the common origin of the spontaneous and symptomatic varieties of zoster. In discussing the association of zoster and facial palsy the authors might have mentioned the first supporting serological evidence reported by Aitken and Brain (*Lancet*, 1933.i.19).

A chapter is devoted to smallpox, cow-pox and vaccinia and the multi-pressure technique of vaccination is clearly described and superlatively illustrated. The better synonym for Kaposi's varicelliform eruption when due to vaccinia virus is surely "eczema vaccinatum" and not "disseminated vaccinia", which merely implies generalized vaccinia and does not conform with Kaposi's description quoted on p. 52.

Warts are given comprehensive review and the wide field of treatment, including psychotherapy, is adequately dealt with. New observations are given on the structure of the viral particles of molluscum contagiosum, which resemble lump sugar in the electron micrograph. Amongst the group of viral diseases contracted from animals, dermatologists will find most interest in milker's nodes and orf. In the later chapters good descriptions of lymphogranuloma venereum, spotted fever and scrub typhus catch the attention.

The excellence of the coloured plates is due to the co-operation of the larger drug houses, which alone can afford the expense of first class colour reproductions. Without such help it would be impossible to attain an economic production of such chromatic merit.

R. T. B.

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* *Viral and Rickettsial Diseases of the Skin, Eye and Mucous Membranes of Man.* By Harvey Blank and Geoffrey Rake. (1955) London: J. & A. Churchill Ltd. Price £3. Pp. 285. 36 Illustrations in colour; 63 black and white.

Occupational and Related Dermatoses.*

This publication consists of short abstracts of 1170 articles which have appeared in the world literature from 1943 to 1953. As its title implies, the abstracts are mainly on occupational subjects. This is a publication which should perhaps appear more often, since abstracts which are now as much as twelve years old are not of such value as they might have been had they been published earlier. The abstracts are in general shorter than those which appear in the Year Book of Dermatology, which otherwise includes very much the same field. A disadvantage of the present publication is that, although there is a brief table of contents, there is no index.

R. F. B.

The VIth International Leprosy Congress.†

This volume is the record of the VIth International Leprosy Congress held in Madrid in October 1953. Three hundred pages are devoted to the therapy of leprosy and the relative merits of the sulphones, thiosemicarbazone, isoniazid and chaulmoogra oil are all discussed. The remaining sections deal with the immunology, bacteriology and epidemiology of leprosy with chapters on classification and the social services. The text occupies 1344 pages, well illustrated with photomicrographs and photographs of clinical cases.

H. T. H. W.

Finger-print Patterns.‡

The finger and palmar prints of mankind have only one basic pattern, but in monkeys the pattern varies with the species. Marks peculiar to lemurs are sometimes found in man. They are atavistic signs that seem to occur particularly in degenerates and most often on the middle finger. In examining the prints of 4187 Cuban criminals the author found the stigma in 13·28% of them. Is this a vindication of Lombroso's old-fashioned opinions?

G. W. B.

A small book on medical aspects of finger-prints§ has also been translated into Spanish by Dr. Israel Castellanos, whose own book was reviewed in this journal (**66** : 70). The information is similar though much less detailed. The print is good and the illustrations very clear.

G. W. B.

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* *Occupational and Related Dermatoses* 1954. Public Health Bibliography Series No. 12 Washington : U.S. Government Printing Office.

† *Memoria del VI Congres. Internacional de Leprologia*, 1953. Madrid (1954) ; Escuela Nacional de Sanidad.

‡ *Estigmas Atavicos en Dermopapiloscopia.* By Israel Castellanos. (1955). P. Fernández y Cia : La Habana. Pp. 152. Illus. 129.

§ *Dactyloscopia y Medicina.* By Dr. Juan Pablo Vieira. (1954). P. Fernández y Cia : La Habana. Pp. 92. Illus. 48.

CORRESPONDENCE.

The Editor, "The British Journal of Dermatology."

Ocular Pemphigus.

Sir,—Church and Sneddon's paper (1953, **65**, 235) on Ocular Pemphigus has greatly contributed to our understanding of the disease. A number of cases of this disease in non-Jewish patients has been observed in U.S.A. In view of the involvement of many mucous membranes throughout the body, even to the exclusion of the conjunctivae in some cases, "ocular pemphigus" should better be called "essential shrinkage of the mucous membranes".

I am writing to you today to call your attention to a possible clue concerning the aetiology of this disease, and it lies in the nature of this clue that it could be better evaluated by Irish, English and Scottish than by American dermatologists. The following incident occurred: At a presentation of two elderly Irish women suffering from the disease at the New York Academy of Medicine, Section on Dermatology (April, 1955) they became acquainted with each other and discovered that they were born in the same county (Sligo) in Ireland and had the same maiden name (Meehan).

From this information I have gathered that this systemic disease may have a genetic background and that my two patients and perhaps others suffering from the disease may have a common ancestor. To my regret I am unable to instigate a search in Irish church registers in order to find out if these two women are actually related to each other because one of them, believing that there is something shameful about the disease, refuses to give me any pertinent data about her family.

In looking over the literature on this disorder I find several reports on Anglo-Saxon patients (Cooper, W. (*Roy. Lond. Ophth. Hosp. Reps.* **1** : 155, 1857–59); Rycroft, B. W. (*Brit. J. Ophth.* **18** : 571, 1934); Church and Sneddon, *Ibid.*; and B. Kanee (*Arch. Derm. Syph., Chicago*, **55** : 37, 1947). Two of my patients (unpublished reports), however, were of Italian descent, but notes on the parentage of patients in U.S.A. are usually not based on any thorough study of family pedigrees. I may add that the statements of the two Irish women that they apparently were not related to each other and that to their knowledge no other member of their respective families showed the same disorder does not eliminate the possibility of a genetic background of the disease.

I hope that dermatologists in Ireland, England and Scotland may confirm my impression that a significant proportion of patients suffering from ocular pemphigus are born in the British Isles and that evidence relevant to the question whether or not there is a genetic basis for the disease may be found.

I am, Sir,
Yours,
Helen Ollendorff Curth, M.D.

New York,
May 1955.

CURRENT LITERATURE.

ORMONAL EFFECTS ON SEBACEOUS GLANDS IN THE WHITE RAT. II: THE EFFECT OF THE PITUITARY ADRENAL AXIS. N. Lasher, A. L. Lorincz and S. Rothman. (1955) *J. invest. Derm.*, **22**, 25.

The testicular androgens have been blamed for acne in males because while eunuchs never have ne it can be evoked in them and in normal subjects by giving testosertone. The conclusion as therefore drawn that the adrenal androgens must be responsible for acne in girls although nuchs and ovarian-deficient females are known to have normal amounts; and, of course, CTH can provoke some sort of an acne, albeit incomplete in regard to seborrhoea and comedones.

In the first experiments with spayed white rats progesterone was as effective as testosterone in using sebaceous hypertrophy. A later trial of various combinations of oophor- adrenal- and pophysectomy with testo- and progesterone revealed that (1) removal of the pituitary leads to sebaceous gland atrophy which cannot be counteracted by progesterone, (2) removal of adrenals so leads to a lesser degree of atrophy which may be partly controlled by progesterone, and that) these operations also reduce the response of the sebaceous glands to testosterone.

The measurement of sebaceous gland volume was effected by planimetry of the gland outlines each of many serial sections projected with magnification on to a screen. The planimeter mploys the principle that the area of any rectangle is the product of two adjacent sides: thus a ller 3·8 in. in diameter and a foot long would cover a square foot with each rotation. But in der to facilitate movement in the second dimension we have, instead of the roller, a rod with a pinter at one end and a wheel that also slides at right angles to its plane of rotation. To any one several points in the rod can be pivoted a link the other end of which turns about a fixed point. he pointer having traced an outline the area contain within it must be the product of the integral tation of the wheel and a factor associated with the position of the pivot. The reviewer is ven to understand that the method affords greater accuracy than the simple one employing uared paper.

In the discussion that followed both papers it clearly emerged that these findings do not uminate very much the clinical problems of acne in man. J. H. T. D.

LTERNATIVE ANTIBIOTICS. F. C. O. Valentine. (1955) *Practitioner*, **29**, 17.

The sensitivity of a bacterial strain is established by cultural methods in the laboratory, and though such sensitivity usually indicates that the drug will be valuable in treatment there e exceptions. Penicillin and streptomycin are bactericidal, whereas chlortetracyclin and xytetracyclin are bacteriostatic only and in certain types of infection a bactericidal drug is ssential. Combination of a bactericidal and bacteriostatic drug may interfere with the action both; on the other hand, combination of two bacteriostatic drugs may result in a synergistic tion. The widespread use of antibiotics will result in the dissemination of a resistant staphylo- cci. In general the application to the skin of an antibiotic suitable for systemic administration ould be avoided as far as possible. The risks attending their use may be due to a direct toxic tion or allergic sensitization. Superinfection with either a yeast or resistant staphylococci using a pseudomembranous enterocolitis is rare but often fatal and chemotherapy can interfere ith the immunity upon which ultimate cure may depend. For superficial staphylococcal infection ugs unsuitable for systemic administration are preferred. *Streptococcus pyogenes* is extremely nsitive to penicillin and has shown no sign of becoming resistant. Viruses, other than the ittacosis group, are not controlled by antibiotics. R. J. C.

TUDIES ON WASH-POWDER DERMATITIS. P. Kroepfli and R. Schuppli. (1955) *Dermatologica*, **110**, 1.

The observation that a number of persons suffering from dermatitis due to a certain wash- owder (" XYZ ") also suffered from stocking-suspender dermatitis caused the authors to make xtensive tests with wash-powders, nickel sulphate, potassium dichromate and other substances. was shown that the majority of these women patients who were positive to " XYZ " were also nsitive to nickel, and a few to chromium, and that numerous other modern wash-powders must so contain Ni and Cr. Furthermore, in 5 out of 8 masons who were known to react positively potassium dichromate, a patch-test with " XYZ " was also positive. J. F. S.

ARTIFICIAL RESIN DERMATITIS. R. Schuppli. (1955) *Dermatologica*, **110**, 7.

In a factory for artificial resins numerous cases of dermatitis occurred which were caused partly by the resins and partly by a substance used for hardening. Patch-testing of all those working with these substances showed that those suffering from dermatitis, and especially those with severe symptoms, were sensitive to numerous other allergens in addition to the resin or hardener, so that the individual disposition is of considerable importance. Appropriate prophylactic measures could therefore be taken. J. F. S.

OLD AND NEW INVESTIGATIONS ON THE SO-CALLED BLACK DERMOGRAPHISM. W. Soltermann. (1955) *Dermatologica*, **110**, 16.

The author has investigated closely the fact that the skin in the region of contact with a metal ornament often acquires a black colour from rubbing. This darkening can be caused by a number of metals so long as there is a substance on the skin, in the form of a powder, salve or paste, that is harder than the metal in question. According to the author's investigations (which included the use of the electron-microscope), the so-called black skin-writing, dermographismus niger, is the result of a purely mechanical process in which the skin plays only the part of a suitable background. J. F. S.

FOLLOW-UP IN CASES OF TUBERCULIDE. G. Miescher. (1955) *Dermatologica*, **110**, 23.

In connection with the catamnestic investigations undertaken by Strauss in the Zurich Clinic, the author discusses the pathogenesis of tuberculides and argues that these are an expression neither of an increased allergy nor of a special form of allergy. Their occurrence is rather the natural result of reciprocal effects between the degree of distribution (number of microbes) and the immunizatory resistance of the skin. The foci of distribution were not clinically demonstrable in the great majority of cases. The dissemination can therefore be only of very limited extent. That it is successful in spite of this suggests a low degree of infection immunity at the site of success. The catamnesis showed that after regression of the tuberculides there was a state of rest, or a tuberculous process became active at some place later, and might even prove fatal. Therefore the tuberculosis present when a tuberculide occurs must be treated with all the means at our disposal. J. F. S.

FOUR CASES OF BOECK'S SARCOID. M. Golay, R. Paillard and W. Jadassohn. (1955) *Dermatologica*, **110**, 31.

On the basis of four cases of Boeck's sarcoid the authors draw attention to the following peculiarities:

(1) In one case the skin changes only appeared three and a half years after the discovery of lung changes.

(2) In one case, in which the definite diagnosis of sarcoid was made on the basis of the lung findings, histologically "lupoid" skin changes could be determined.

(3) In one case, sarcoid and partly "lupoid" skin efflorescences appeared from ten to nineteen years after scars from bicycle accidents had been acquired. Birefractory crystals could not be found. The foci disappeared on arsenic treatment.

(4) In one case, the disseminated efflorescences showed confluence in places, and erythematous areas. The histological picture showed slight response to streptomycin-cortisone treatment.

(5) In two cases the sarcoid tubercles were very superficially sub-epidermal, with epidermal changes—atrophy, disappearance of the interpapillary rete pegs and depigmentation—an observation which leads to a discussion of the differential diagnosis between Boeck's sarcoid and lichen nitidus. J. F. S.

KYRLE'S DISEASE. P. de Graciansky, S. Roulle, M. Boulle and J. Dalion. (1955) *Ann. Derm. Syph., Paris*, **82**, 8.

A review is presented of 29 published cases with illustrations together with a previously unpublished account. The authors only accept 12 cases as authentic, the others being doubtful or inadequately reported. The essential features, in addition to the clinical appearance, are the penetration of a horny mass into the dermis through a gap in the germinal layer or evidence that such is about to happen. The presence of a dermal foreign body reaction depends on the degree and duration of the penetration. They suggest that the condition may be a "genodermatose" and classed with Darier's disease and pityriasis rubra pilaris. F. F. H.